Abstracts of the papers of Aneliya Kostadinova for participation in the concourse for the academic position „Associated professor"

I. Publications in Indicator B4

1. Groth T, Seifert B, Malsch G, Albrecht W, Paul D, Kostadinova A, Krasteva, N., Altankov G. (1999). Altered vitronectin receptor (alpha-v integrin) function in fibroblasts adhering on hydrophobic glass. Journal of Biomedical Materials Research, 44(3), 341-351.
IF-2.038 (Q1 WebS)

Function of integrins is crucial for adhesion, movement, proliferation, and survival of cells. In a recent study we found impaired fibronectin receptor function on hydrophobic substrata (G. Altankov et al. J Biomater Sci Polym Edn 1997;8:712–740). Here, we have studied the distribution and function of the vitronectin receptor (av integrin) in fibroblasts adhering on hydrophilic glass and hydrophobic octadecyl glass (ODS). The morphology of fibroblasts and the organization of actin cytoskeleton were studied and found to be altered on ODS, where the cells did not spread and possessed condensed actin. Pretreatment of the surfaces with serum or pure vitronectin improved cell morphology on both substrats, resulting in the development of longitudinal actin stress fibers. It was found with biotinylated vitronectin that comparable quantities of vitronectin were adsorbed from single vitronectin solutions or serum on glass and on hydrophobic ODS. The organization of the vitronectin receptors on the ventral cell surface was investigated in permeabilized cells showing normal focal adhesions in fibroblasts plated on glass but none of these structures on ODS. The distribution of av integrin on the dorsal cell surface was studied on nonpermeabilized living cells after antibody tagging. While fibroblasts adhering on plain or serum-treated glass developed a linear organization of av integrin, cells on plain and serum-treated ODS were notable to reorganize the vitronectin receptor. Studies on signal transduction with antiphosphotyrosine antibodies revealed co-localization of av integrin and phosphotyrosine in focal adhesions on glass and serum-treated glass. However, signaling was almost absent on plain ODS and weak on serum-treated ODS. It was concluded that alterations in vitronectin receptor function on the ventral cell surface caused by the hydrophobic material surface inhibit signal transfer and subsequent intracellular events that are important for the organization and function of integrins

2. Groth Th., Altankov G, Kostadinova A, Krasteva N,, Albrecht W, Paul D. (2002). Interaction of human skin fibroblasts with moderate wettable polyacrylonitrile-copolymer membranes. Journal of Biomedical Materials Research, 61(2), 290-300. ISI IF-1.950 (Q1)

The development of a bioartificial skin is a step toward the treatment of patients with deep burns or nonhealing skin ulcers. One possible approach is based on growing dermal

cells on membranes to obtain appropriate living cellular stroma (sheets) to cover the wound. New membrane-forming copolymers were synthesized, based on acrylonitrile (AN) copolymerization with hydrophilic N-vinylpyrrolidone (NVP) monomer, in different percentage ratios, such as 5, 20, and 30% w/w, and with two other relatively high polar comonomers – namely, sodium 2-methyl-2-propene-1-sulfonicacid (NaMAS) and aminoethylmethacrylate (AeMA). All these copolymers were characterized for their bulk composition and number average molecular weight, and used to prepare ultrafiltration membranes. Water contact angles and water uptake were estimated to characterize the wettability and scanning force microscopy to visualize the morphology of the resulting polymer surface. Cytotoxicity was estimated according to the international standard regulations, and the materials were found to be nontoxic. The interaction of the membranes with human skin fibroblasts was investigated considering that the cells are among the first to colonize membranes upon implantation or with prolonged external contact. The overall cell morphology, formation of focal adhesion contacts, and cell proliferation were estimated to characterize the cell material interactions. It was found that the pure polyacrylonitrile homopolymer (PAN) membrane provides excellent conditions for seeding with fibroblasts, comparable only to a copolymer containing AeMA. In contrast, the presence of NaMAS with acidic ionic groups decreased both the attachment and proliferation of fibroblasts. Low content of NVP in the copolymer, up to about 5%, still enabled good attachment and spreading of cells, as well as subsequent proliferation of fibroblasts, but higher ratios of 20 and 30% resulted inasignificant decrease of the cellular activities

3. Madalina G. Albu, Todorka G. Vladkova, Iliana A. Ivanova, Ahmed S. A. Shalaby, Moskova-Doumanova, V., Anna D. Staneva, Yanko B. Dimitriev, Anelya S. Kostadinova, Tanya I. Topouzova-Hristova (2016). Preparation and Biological Activity of New Collagen Composites, Part I: Collagen/Zinc Titanate Nanocomposites. Applied Biochemistry and Biotechnology, 180(1), 177-193. ISI IF:1.606 (Q2)

The aim of this investigation was to develop new antimicrobial collagen/zinc titanate (ZnTiO3) biomaterials using a sol–gel cryogenic draying technology in keeping the native collagen activity. Broad-spectrum antimicrobial activity was demonstrated against Firmicutes (*Staphylococcus epidermidis*, *Bacillus cereus*, and *Candida lusitaniae*) and Gracilicutes (*Escherichia coli*, *Salmonella enterica*, and *Pseudomonas putida*) microorganisms. The antimicrobial activity as well as the cytotoxicity were specific for the different test microorganisms (Gram-positive and Gram-negative bacteria and fungi) and model eukaryotic cells (osteosarcoma, fibroblast, and keratinocyte cells), respectively, and both were depending on the ZnTiO3 concentration. Three mechanisms of the antimicrobial action were supposed, including (i) mechanical demolition of the cell wall and membrane by the crystal nanoparticles of the ZnTiO3 entrapped in the collagen matrix, (ii) chelation of its metal ions, and (iii) formation of free oxygen radicals due to the interaction between the microbial cells and antimicrobial agent. It was concluded that the optimal balance between antimicrobial activity and cytotoxicity could be achieved by a variation of the ZnTiO3 concentration. The antifungal and broad-spectrum antibacterial activity of the studied collagen/ZnTiO3 nanocomposites, combined with a low cytotoxicity, makes them a promising anti-infection biomaterial.

4. Kostadinova, A., Doumanov, J., Moyankova, D., Ivanov, S., Mladenova, K., Djilianov, D., & Topouzova, T. (2016). Haberlea rhodopensis extracts affect cell

periphery of keratinocytes. Comptes rendus de l'Acad´emie bulgare des Sciences, 69, 4, 439-448. ISI IF:0.234 (Q3)

Common features of chronic dermatological conditions are inflammation and ROS overgeneration, as well as disturbances in cell proliferation and di ferentiation. Our aim was to study the impact of *Haberlea rhodopensis* extracts on the mitochondrial activity, integrity of cell membranes, actin cytoskeleton and tight junctions (the loss of ZO-1 protein) of the human keratinocytes (HaCaT cells). Cytotoxity tests such as MTS, LDH assay and trypan blue exclusion assay were performed to evaluate metabolic activity and membrane permeability of the cells. In concentrations up to 2 mg/ml the extracts influence cell periphery, permeabilize the membrane and disrupt tight junctions of HaCaT keratinocytes, which is more pronounced in actively dividing cells (Ca+ cells). Our results show that extracts of *Haberlea rhodopensis* could be a good candidate to be used in complex treatment of pathological dermatological conditions.

5. Kostadinova, A., Hazarosova, R., Topouzova-Hristova, T., Moyankova, D., Yordanova, V., Veleva, R., Djilianov D., Momchlova A., Staneva, G. (2022). Myconoside interacts with the plasma membranes and the actin cytoskeleton and provokes cytotoxicity in human lung adenocarcinoma A549 cells. Journal of Bioenergetics and Biomembranes, 54(1), 31-43 .IF 2,740.(Q2)

Studies have been carried out on the effects of the phenyl glycoside myconoside, extracted from the relict, Balkan endemic resurrection plant *Haberlea rhodopensis* on the plasma membrane structural organization and the actin cytoskeleton. Because the plasma membrane is the first target of exogenous bioactive compounds, we focused our attention on the influence of myconoside on the membrane lipid order and actin cytoskeleton in human lung adenocarcinoma A549 cells, using fluorescent spectroscopy and microscopy techniques. We found that low myconoside concentration (5 μg/ml) did not change cell viability but was able to increase plasma membrane lipid order of the treated cells. Higher myconoside concentration (20 μg/ml) inhibited cell viability by decreasing plasma membrane lipid order and impairing actin cytoskeleton. We hypothesize that the observed changes in the plasma membrane structural organization and the actin cytoskeleton are functionally connected to cell viability. Biomimetic membranes were used to demonstrate that myconoside is able to reorganize the membrane lipids by changing the fraction of sphingomyelin-cholesterol enriched domains. Thus, we propose a putative mechanism of action of myconoside on A549 cells plasma membrane lipids as well as on actin filaments in order to explain its cytotoxic effect at high myconoside concentration.

II. Publications in Indicator Г 7

1. Kostadinova, A., Zaekov, N., & Keranov, I. (2012). Interaction of cells with modified polyethylenglycol surfaces. Bulgarian Journal of Agricultural Science, 19, 178-181. SJR (Scopus): 0.163 (Q3)

The uses of biomaterials based on polymers, contacting with the living tissue, blood, proteins and other biological fluids inside or outside of the human body requires solving serious problems with biocompatibility. The problems could be overcome with appropriate polymer surface modification, introducing various functional groups, positively charged, negatively charged and uncharged. The aim of this work is to improve the surface biocompatibility of hydrophobic poly (dimethylsiloxane) (PDMS), using plasma treatment followed by acrylic acid grafting with different density and PEG coupling with different density and chain length. The maximum of cell adhesion and proliferation on the surface with an average density of PEG were observed.

2. Nikolova,B., Kostadinova,A.,Dimitrov,B., ZhelevZ., Bakalova R., Aoki I., Tsuneo Saga, Tsoneva I. (2013). Fluorescent imaging for assessment of the effect of combined application of electroporation and rifampicin on HaCaT cells as a new therapeutic approach for psoriasis. Sensors, 13(3), 3625-3634. ISI IF:1.739 (Q2)

The study aimed to clarify the role of electric pulses in combination with chemotherapy on the viability of keratinocyte cell line HaCaT, in the context of its application as a new therapeutic approach for psoriasis. The data show that electroporation of HaCaT cells in combination with rifampicin induces cytoskeleton disruption and increases permeability of cell monolayer due to cell-cell junctions interruption, visualized by fluorescent imaging of E-cadherin and actin integrity. This was accompanied with synergistic reduction of cell viability. The study proposes a new opportunity for more effective skin treatment than chemotherapy. The future application of this electrochemotherapeutic approach for combined local treatment of psoriasis may have serous benefits because of a high possibility to avoid side effects of conventional chemothera.

3. Kostadinova, A., Nikolova, B., Handjiiska, P., Berger, M., & Tsoneva, I. (2015). Combined effect of electroporation and miltefosine on keratinocyte cell line HaCat. Romanian Reports in Physics, 67, 995-1003 ISI IF:1,367(Q2)

In this study we investigated the effect of combined treatment of HaCaT keratinocyte cells with electrical pulses (200 – 500 V/cm) and the alkylphosholipid (ALP) miltefosine. The data show that electroporation in combination with miltefosine induces cytoskeleton disruption and increases the permeability of cell monolayers due to interruption of cell-cell junctions, as documented by fluorescent imaging of ZO-1 and actin integrity. This was accompanied with reduction of cell viability. The combination of these conditions could be considered as a method for treating several types of skin cancer or other pathological conditions affecting the skin integrity.

4. Kostadinova, A., Topouzova-Hristova, T., Momchilova, A., Tzoneva, R., & Berger, M. R. (2015). Antitumor Lipids—Structure, Functions, and Medical Applications Advances Protein Chemistry and Structural Biology ., 101, Elsevier, 2015, ISBN:1876-1623 ISI IF:3.736(Q1) Advances in Protein Chemistry and Structural Biology, Volume 101, 2015 Elsevier Inc. ISSN 1876-1623 All rights reserved. http://dx.doi.org/10.1016/bs.apcsb.2015.08.001

Cell proliferation and metastasis are considered hallmarks of tumor progression. Therefore, efforts have been made to develop novel anticancer drugs that inhibit both the proliferation and the motility of tumor cells. Synthetic antitumor lipids (ATLs), which are chemically divided into two main classes, comprise (i) alkylphospholipids (APLs) and (ii) alkylphosphocholines (APCs). They represent a new entity of drugs with distinct antiproliferative properties in tumor cells. These compounds do not interfere with the DNA or mitotic spindle apparatus of the cell, instead, they incorporate into cell membranes, where they accumulate and interfere with lipid metabolism and lipid-dependent signaling pathways. Recently, it has been shown that the most commonly studied APLs inhibit proliferation by inducing apoptosis in malignant cells while leaving normal cells unaffected and are potent sensitizers of conventional chemo and radiotherapy, as wellas of electrical fieldtherapy. APLs resist catabolic degradation to a large extent, therefore accumulate in the cell and interfere with lipid-dependent survival signaling pathways, notably PI3K-AktandRaf-Erk1/2, and denovo phospholipidbiosynthesis. They are internalized in the cell membrane via raft domains and cause downstream reactions as inhibition of cell growth and migration, cell cycle arrest, actin stress fibers collapse, and apoptosis. This review summarizes the in vitro, in vivo, and clinical trials of most common ATLs and their mode of action at molecular and biochemical levels.

5. Kostadinova, A., Georgieva, I., Topouzova, T., & Tzoneva, R. (2016). Effect of electrical field and miltefosine on actin and actin-associated protein ZO-1 organization in cancer and non cancerous cells. Comptes rendus de l'Acad´emie bulgare des Sciences, 69, 585-592. (Q3)

The actin cytoskeleton plays a key role in the stability of cell-cell junctions, adhesion and cell motility, which are crucial for tumour progression and metastases. Changes in the actin filaments organization could affect and increase permeability of cell monolayer due to interruption and reorganization of tight junctions in epithelial cells. In this study we investigate the combined effect of the electrioporation and miltefosine on the F-actin and ZO-1 in cancer epithelial line A549 and non-cancer cell line MDCKII. Our results showed that treatment of A549 and MDCK cells with electrical field in combination with miltefosine is cell-specific. The cancer A549 cell line was found to be more sensitive to the treatment as compared to non-cancerous cells. Actin cytoskeleton was highly disturbed while ZO-1 organization seems stabilized.

6. Nikola Mladenov, Svetla D. Petrova, Kirilka Mladenova, Desislava Bozhinova, Veselina Moskova-Doumanova, Tanya Topouzova-Hristova, Pavel Videv, Ralitsa Veleva, Aneliya Kostadinova, Galya Staneva, Tonya D. Andreeva, Jordan Doumanov (2020). Miscibility of hBest1 and sphingomyelin in surface films – A prerequisite for interaction with membrane domains. Colloids and Surfaces B: Biointerfaces, 189, 110893. doi:10.1016/j.colsurfb.2020.110893 (Web of Science) IF:4.389(Q1)

Human bestrophin-1(hBest1) is a transmembrane Ca2+-dependent anion channel, associated with the transport of Cl−, HCO3- ions, γ-aminobutiric acid (GABA), glutamate (Glu), and regulation of retinal homeostasis. Its mutant forms cause retinal degenerative diseases, defined as Bestrophin opathies. Using both physicochemical surface pressure/mean molecular area (π/A) isotherms, hysteresis, compressibility moduli of hBest1/sphingomyelin (SM) monolayers, Brewster angle microscopy (BAM) studies, and biological approaches - detergent membrane fractionation, Laurdan (6-dodecanoyl-N, N-dimethyl-2-naphthylamine) and immunofluorescence staining of stablytransfected MDCK-hBest1 and MDCKII cells, we report: 1) Ca2+, Gluand GABA interact with binaryhBest1/SMmonolayersat35°C, resulting in changes in hBest1 surface conformation, structure, self-organization and surface dynamics. The process of mixing in hBest1/SM monolayers is spontaneous and the effect of protein on binaryfilms was defined as "fluidizing", hindering the phase-transition of monolayer from liquid-expanded to intermediate (LE-M) state; 2) in stablytransfected MDCK-hBest1cells,bestrophin-1was distributed between detergent resistant (DRM) and detergent-soluble membranes (DSM) - up to 30 % and 70 %, respectively; in alive cells, hBest1 was visualized in both liquid-ordered (Lo) and liquid-disordered (Ld) fractions, quantifying protein association up to 35 % and 65 % with Lo and Ld. Our results indicate that the spontaneous miscibility of hBest1 and SM is a prerequisite to diverse protein interactions with membrane domains, different structural conformations and biological functions**.**

7. Yankova, R., Kostadinova, A., & Radev, L. (2020). DFT calculations, characterization and in vitro cytotoxicity of platinum(II) complex of 3-amino-1,2,4-triazole. 965-978 Journal of Chemical Technology and Metallurgy, ISSN:1314-7978, 965-978. SJR (Scopus):0.190(Q3)

A platinum(II) complex of 3-amino-1,2,4-triazole is synthesized and characterized by using 1H, 13C NMR and FT-IR spectroscopies. The molecular geometry and the chemical reactivity of the complex are studied using the Density Functional Theory at B3LYP/6-311++G(d,p) basis set of H, C, N, Cl and LANL2DZ for Pt. The molecular electrostatic potential surface, the natural bond orbital and the natural charge population are estimated. The frontier molecular orbital analyses are conducted. The intramolecular interactions in [Pt(3-amino-1,2,4-triazole)$_2$Cl$_2$] are investigated using the quantum theory Atoms in Molecules. It is observed that the complex is stabilized via two hydrogen bonds, N–H···Cl, which are weak and electrostatic in nature. They determine the different energy and bond length of Pt–Cl and Pt–N. The compound cytotoxicity is evaluated using 2 type eukaryotic cells: MDCK II kidney epithelial cell line and A549 cancer alveolar cell line. The results of this investigation demonstrate the high cytotoxic effect of [Pt(3-amino-1,2,4-triazole)$_2$Cl$_2$] especially to cancer cells. This Pt(II) complex is a promising nanomaterial for a variety of biomedical applications, including cancer therapy.

8. Ivanova I., Stoyanova D., Nenova E., Kostadinova A., Staneva A. Antimicrobial and cytotoxic properties of graphene and metal nanomaterials. Journal of Chemical Technology & Metallurgy, 55, 2, w, 2020, ISSN:1314-7978, SJR (Scopus):0.190(Q3)

The nanotechnology is the fastest developing branch of science in the border of physics, chemistry, biology and electronics. The ecological effect of nanomaterials on various organisms is still not enough understood. This review of the literature presents the mechanisms of action of nanomaterials: eluted metal ions, size and form of nanoparticles, reactive oxygen species and non-ionic interactions. The results obtained by different authors on the effects of graphene, metal nanoparticles, their oxides and nanocomposites on different types of organisms - prokaryotes and eukaryotes are described. Antimicrobial and cytotoxic properties of the new materials are discussed in respect to their medical and environmental significance.

9. Yankova, R., Kostadinova, A., Toshkovska, R., & Ivanova, I. (2020). Characterisation and in vitro cytotoxicity of silver(I) benzimidazole complex. Oxidation Communications, 43, 647-660 SJR (Scopus):0.224(Q3)

Chemical structure and biological activity of silver(I) complex of benzimidazole were investigated. The complex was synthesised using EtOH solution of the silver nitrate and benzimidazole and precipitation product was purified and vacuum dried. FTIR spectroscopy and Powder X-ray diffraction was used to confirm the phase purity of the synthesised material. The intramolecular chemical bonds nature was described. The antibacterial effect of the complex was evaluated against Gram-negative *E. coli* ATCC25922 and Gram-positive Staphylococcus aureus ATCC 25923 and compared with $AgNO_3$ and previous synthesised Pt(II) 3-amino-1,2,4-triazole complex. The Gram-positive *S. aureus* have shown higher sensitivity than *E. coli*, famous with their efflux cells pumps used for protection of metal ions and antibiotics. The silver complex did not inhibit the fungus *Candida lusitaniae* grown in *Sabouraud dextrose* medium. Cytotoxic activity of the complex was examined against two types of cell lines: cancer (A549) and noncancerous eukaryotic cell (MDCK). All of the tested silver(I) complex concentrations were toxic for cancer cell line and without effect on normal cells till 5 μg/ml. In concentration from 10 to 50 μg/ml silver(I) complex kills almost 70% of cancerous cells, but also normal epithelial cells are influenced at 50%. It can be concluded that silver(I) benzimidazole complex effects on the different way with cancer and noncancerous cells. In the same time, the synthesised silver benzimidazole compound has well demonstrated antibacterial effect in concentration of 10 μg/ml. In contrast, platinum(II) 3-amino-1,2,4-triazole complex has no toxic effect on both bacteria and the fungus tested. This specific effect of silver(I) benzimidazole complex could be used in medical application like substance that specifically kills epithelial cancer cells (skin melanoma, lung and kidney cancer, etc.).

10. Kostadinova, A., Keranov, I., Vladkova, T., Michel, M., Ivanova, I., & Yankova, R. (2020). Characterisation and biological response of electrospun amphiphilic poly (dimethylsiloxane-b-acrylic acid) fibrous scaffolds. Oxidation Communications, 43, 234-247. SJR (Scopus):0.224(Q3)

The obtaining of poly (dimethylsiloxane-block-acrylic acid) (PDMS-b-PAA) fibres scaffold driven by electrospinning, one of the most versatile and powerful physicalchemical methods is described. The process was controlled by varying of voltage,

flow rate, collector-to-tip distance and polymer solution concentration. The new fibres mats were characterised by numerous methods as follows: Scanning electron microscopy (SEM), Differential scanning calorimetry (DSC), and Water contact angle (WCA). The influence of the fibre scaffold morphology on in vitro biocompatibility was investigated by culturing cells on the scaffolds, immunofluorescence and MTT assay. The results indicated that the keratinocytes could attach and proliferate on the unique scaffolds, which confirmed that the PDMS-b-PAA amphiphilic mat had good biocompatibility, and it could be a promising biomaterial for tissue engineering applications.

11. Kostadinova, A., Staneva, G., Benkova, D., Yordanova, V., Hazarosova, R., Veleva, R., Nesheva, A., Momchilova, A., Yankova, R., Elzorkany, H., Elshoky, H. (2021). Interaction of chitosan-based nanoparticles with bio-inspired membranes. Oxidation Communications, 44, 63-71. SJR (Scopus):0.224(Q3)

Chitosan is a natural copolymer derived from the deacetylation of chitin. Because of its specific physicochemical properties, chitosan is a perfect material to be used in bioengineering and biomedicine. In this study, we demonstrated how chitosan is able to affect the lipid order and organisation in biomimetic membranes. We formed large unilamellar vesicles (LUVs) composed of different lipids and their mixtures mimicking the lipid architecture of mammalian plasma membranes. Lipid order was probed by Laurdan spectroscopy measurements at physiological temperature. We studied LUVs composed of egg phosphatidylcholine (ePC) exhibiting lipid bilayer in liquid-disordered phase (Ld), egg sphingomyelin (eSM)/cholesterol (Chol) in liquid-ordered phase (Lo), and ePC/eSM/ Chol mixtures representing Ld/Lo phase coexistence. The ternary mixture compositions mimic the plasma membrane organisation and formation of raft-like domains with different sizes. Membrane rafts are known to be involved in crucial cellular physiological events in health and disease. LUVs were treated by increasing chitosan concentration and lipid order was assessed by Laurdan fluorescence spectroscopy. The interaction of chitosan with lipid membranes induces an increase in the lipid order independently of the lipid phase state. The highest increase in the lipid order was observed for the Ld phases, whereas, the lowest one was detected for the Lo phase. We suggested molecular mechanisms of interaction of chitosan with the main lipid classes and their phase state.

12. Kichukova, Diana, Ivanka Spassova, Aneliya Kostadinova, Anna Staneva and Daniela Kovacheva. 2022. "Facile Synthesized Cu–RGO and Ag–RGO Nanocomposites with Potential BiomedicalApplications"*Nanomaterials,* 12, no.12:2096. ISSN:2079-4991 https://doi.org/10.3390/nano12122096 Web Sci IF: 5.076(Q1)

In the present study, we report on the facile prepared nanocomposites of reduced grapheme oxide RGO with Cu and Ag. The synthesis was performed through an environmentally friendly and easy method by simultaneous reduction in solutions containing Cu^{2+} or Ag^{+} and graphene oxide (GO) using zinc powder as a reducing agent in aqueous acidic media. The composites are characterized by powder X-ray diffraction, low-temperature nitrogen adsorption, X-ray photoelectron and FTIR and Raman spectroscopies, as well as Scanning and Transmission electron microscopies. The antibacterial activity of the composites was tested for *Staphylococcus aureus*, *Escherichia coli* and antifungal activity for *Candida albicans*. The cytotoxicity of the materials was studied towards two types of eukaryotic cells—MDCK II and A549 cell lines. The composites obtained consist of homogeneously distributed Cu and Ag nanoparticles on the surface of graphene sheets and manifest good antimicrobial activity and high

cytotoxicity. The results clearly show that both metal–RGO composites can be successfully used as antimicrobial and anticancer agents.

III. Publications in Indicator Г8

1. Kostadinova A, Keranov I. Modifications of the polymer surface aimed at improvingcell adhesion and interaction.(2019) eBook: Importance & Applications of Nanotechnology Publisher, MedDocs Publishers LLC,Online edition: http://meddocsonline.org, 2019, ISBN: 978-81-941833-0-3

The most commonly used biomaterials are polymers – natural (collagen, laminin, chitosan) or synthetic (polylactide, polyethylene oxide, polyglutamate, etc.), which have certain (appropriate) mechanical properties, but most importantly, they are biodegradable. Chemical polymers have recently been preferred and displaced natural ones such as donor skin, collagen, bone implants, etc., as they are cheaper, easier to modify, and largely avoid immunological reactions. The next stage in the development of biomaterials is related to the emergence of bio-hybrid technologies, with the demand for materials that have a positive response to tissues. These are bioactive biomaterials. They are looking for contact with tissues, looking for ways to optimize these interactions. Exploring cell-surface interaction is important for the creation of both bioinnergic and bioactive (hybrid) materials vital to medicine. Despite the efforts made so far, the mechanism of this impact has not yet been fully elucidated. Functioning of polymer surfaces is an approach recently used systematically to modulate their interaction with living cells. It allows to take a deep look into the mechanisms of biocompatibility and to understand the role of the surface properties of polymeric biomaterials for their successful interaction with the body. The resulting new materials would be of great importance for use in medicine and biomedical engineering.