Chitosan-silver nanocomposites – modern antibacterial materials

Anna REGIEL, Agnieszka KYZIOŁ – Faculty of Chemistry, Coordination and Bioinorganic Physicochemistry Group, Jagiellonian University, Cracow, Poland; Manuel ARRUEBO – Department of Chemical Engineering, Nanoscience Institute of Aragon (INA); Networking Research Center on Bioengineering, Biomaterials and Nanomedicine, CIBER-BBN, E-50018 Zaragoza, Spain

Please cite as: CHEMIK 2013, **67**, 8, 683–692

Introduction

Nowadays there is a great interest in BioNanoMaterials with antibacterial activity against multidrug resistant bacterial strains (MDR-multidrug resistance). Most of conventional antibiotics are not effective anymore. Sometimes mutations, which induce the resistance acquiring, are caused by inconsistent and excessive antibiotics administration. One of the bacterial adaptations is biofilm formation, which constitutes a specific barrier between cells and environmental conditions. Biofilm forming prevents biocide activity of currently applied antibiotics. Compact structure of polysaccharides, proteins and nucleic acids protects bacteria colonies against adverse conditions [1]. As a consequence of increasing resistance, chronic bacterial infections are more often observed (post-operative wounds infections, osteomyelitis, septic arthritis, endocarditis *etc.*). Multidrug resistance has become a global problem, mostly because of the ease of causal pathogens spreading. The ECDE/EMEA (the European Centre for Disease Prevention and Control/the European Medicines Agency) report has pinpointed the most dangerous, antibiotics-resistant bacterial strains: *Staphylococcus aureus* MRSA (methacillin resistance), *Staphylococcus aureus* VISA/VRSA (vancomycin intermediate resistance, vancomycin resistance). Infections induced by these strains often lead to death of many patients [2].

Searching for new therapeutic agents capable to work against resistant bacterial strains is one of the most important challenges for nowadays science. Application of nanotechnology in creating new biomaterials provides new solutions mainly because of small dimensions of the created systems. One of the most effective and promising materials are nanocomposites based on silver nanoparticles (AgNPs) and chitosan.

Chitosan as antibacterial agent?

Structure and main properties

Chitosan is a natural, cationic polysaccharide obtained from chitin. It is the second, after cellulose, most abundant natural polymer [3]. This copolymer consist of β-1,4 – linked N-acetyl-D-glucosamine and D-glucosamine units (Fig.1). Depending on conditions of the deacetylation process (deacetylation of chitin provides chitosan), different forms of chitosan are available. Those forms vary in the deacetylation degree (DD) (indicating the amount of free amino groups) and the average molecular weight (Mw) of the polymer. Both of those features, determine the physicochemical properties of the polymer and its application.

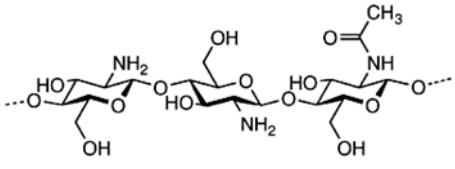

Fig. 1. Chitosan's structure

Due to the presence of functional groups (amino and hydroxyl), chitosan shows many interesting properties [4]. Applications of chitosan are a consequence of its biodegradability, biocompatibility and non-toxicity. Moreover, chitosan exhibits an antibacterial activity against both, Gram-positive and Gram-negative bacterial strains [5]. Its activity was demonstrated at many bacteria, fungi and yeasts [6, 7]. The exact mechanism of antibacterial action of chitosan has not been elucidated yet. There is a hypothesis stating that the source of chitosan antimicrobial activity is its polycationic nature. The interactions between protonated amino groups and negatively charged microorganisms cell wall components lead to the intracellular components leakage. The higher density of positive charge (higher deacetylation degree) the stronger is antimicrobial action [8, 9]. Antibacterial effect might be also a result of chitosan ability of metal ions complexation which deprives bacterial cells of essential components and causes homeostasis disorder [10]. It has been also demonstrated that Mw influences antimicrobial action. Low molecular weight fractions of chitosan can penetrate the cell wall and interact with internal components as DNA, while high molecular weight fractions are rather interacting on the bacterial cell wall surface. In both cases it changes the natural cell conditions and causes irreversible, mortal modifications [11]. Bacterial cell wall composition, different for Gram-positive and Gram-negative, also influences the antimicrobial action strength and mechanism [12]. The possibility of a biocide effect occurrence depends on the chitosan specimen form as well (solution, powder, membrane, *etc.*).

Selected chitosan application

Due to unique properties, chitosan found many commercial applications. The polymer and its derivatives are used as biomaterials in pharmaceutics, cosmetics, medicine, food industries *etc.*. Representative examples are summarized in Table 1.

Table 1

Applications of chitosan

Pharmaceutics
• Gels, hydrogels (controlled, sustained drug release [13, 14]) • Films and membranes (controlled drug release [14]) • Emulsions (microspheres, microcapsules), (sustained drug release, increased bioavailability, mucoadhesion [15]) • Targeted cancer therapy (retention and accumulation of drug in tumor [16]) • Systems for controlled delivery/release of peptide drugs [17], vaccines[18], genes [19]
Medicine and biomedicine
• Wound dressings, wound treatment, bandages [20] • Sutures, surgical implants [21] • Hemodialysis membranes, biomedical devices coatings [22], • Hemostatics [23], anticoagulants [24]
Tissue engineering Scaffolds for tissue engineering, artificial skin grafts [25]
Other: *Agriculture, food industry [26], textile industry [5], wastewater treatment [25]*

Given the large number of chitosan properties, it comes as no surprise that it is still very popular object of scientific research.

Silver nanoparticles – drug or pesticide?

Silver is widely known as antibacterial, antifungal, antiviral and anti-inflammatory agent [27, 28]. Next to the commonly used silver ions based antimicrobial agents, commercially available nanosilver has lately gathered a lot of attention. Nowadays, however nanosilver is present in antibacterial wounds dressings, antibacterial coatings for fridges *etc*., a lot of discussions focus on its probable side effects. Silver nanoparticles exhibit interesting properties such as: tunable size, shape, ease of surface modifications and ability of silver ions release. That makes them suitable for obtaining materials with designed and required properties. What is more, nanoparticles of silver, gold and copper has been presented as agents of high antibacterial activity against many dangerous and resistant bacterial strains [29÷31]. Silver nanoparticles constitute a promising alternative in fighting down chronic bacterial infections, that is why there already exists antibacterial commercial products based on AgNPs [32]. Unfortunately, metal nanoparticles at high concentration level or in direct contact with human cells, exhibit cytotoxicity. It implies that searching for new, less toxic towards healthy human cells materials is still required.

Silver nanoparticles are very interesting for scientists, mainly due to their optic and electric properties which make them suitable for applications in electronics, catalysis, biotechnology and medicine. Because of such a wide range of applications, several physical and chemical methods concerning the fabrication of silver nanoparticles have been developed [33]. Among various methods used for AgNPs preparation, a chemical reduction of silver ions that results in stable colloidal dispersion [34], is the most popular. Sodium borohydride, ascorbic acid or citric acid are typical reducing agents. Selection and control of synthesis parameters (temperature, time, rate of the reagents adding), reducing and stabilizing agent depends on the desired nanoparticles features [35].

Antibacterial activity of silver nanoparticles

The highest antibacterial activity is exhibited by the smallest AgNPs with dimensions less than 10 nm. The smaller they are the higher surface area and therefore surface – to – volume ratio (which makes that its oxidation kinetics increases release of silver ions and consequently shows an enhanced bactericidal action compared to the same bulk material) [36]. They can bind with the bacterial cell wall, but also penetrate the membrane and interact with internal components and as a consequence interfere in a cell homeostasis leading to its death [37]. The mechanism of silver nanoparticles antibacterial activity is very complex. Many studies suggest that AgNPs interact with the cell wall and penetrate the membrane, leading to the cell death [38]. Next to this, the antimicrobial activity of AgNPs is a result of silver ions released from the nanoparticles surface [39]. Released silver ions bind to sulfhydryl groups leading to protein denaturation. Attachment of AgNPs to the bacteria cell, changes its permeability and disturbs functionality. What is more, silver nanoparticles interfere dissipation of the proton motive force [39]. Another possible mechanism of AgNPs antibacterial action is induction of free radicals formation which damages the membrane and causes cell death [30]. Also the dependence of antibacterial activity on the structure of bacterial cell wall is important; Gram–negative bacteria were found to be less resistant for AgNPs activity than Gram–positive strains [39].

Cytotoxicity of silver nanoparticles

Development of nanotechnology forces scientists to debate about the toxicity of nanomaterials. Cytotoxicity of nanoparticles is still an issue thought to be unsatisfactorily examined [40]. Some studies have show that the toxic effect occurs at different levels: cellular, subcellular and biomolecular (proteins, genes) [41]. Proposed mechanism of cytotoxicity establishes and induction of reactive oxygen species (ROS) [42]. Decrease of glutathione level and increase in ROS concentration, leading to lipids peroxydation, have been observed *in vivo* [43]. ROS induce irreversible DNA damages and in consequence apoptosis or necrosis [42, 43]. Undesired AgNPs activity has forced EPA (Environmental Protection Agency) to officially regulate nanosilver administration and consider AgNPs as pesticide [44]. There is still a lot to discover in that matter.

Chitosan-silver nanocomposites

Polymeric nanocomposites are advanced, functional materials based on nanoparticles finely dispersed polymeric matrix or/and covered with polymer (core-shell structures) [45, 46]. Most of the practical applications of AgNPs demand the polymeric or other outer-layer for nanoparticles. Polymers are usually the most suitable matrix due to a specific surface morphology, chain structure enabling nanoparticles incorporation and their homogenous dispersion. In some cases, functional groups of polymer may be responsible for nanoparticles synthesis (chemical reduction) [47]. Designing hybrid nanomaterials, which involves different antibacterial activity mechanisms is ingenious but not effortless. Unfortunately, toxic substances for bacterial cells also often exhibit cytotoxicity against human cells. In that case, substances are not appropriate for medical applications. Thus, nanocomposites should demonstrate some basic features in order to minimize the cytotoxicity:

- fabrication (in macro scale) of biocompatible and non-toxic materials (*e.g*. polymers as chitosan, alginate, *etc*.)
- selective interaction of an active agent with bacterial cells
- materials can not release the excess of a toxic agent to the environment (*e.g*. metal nanoparticles).

Taking into account the minimization of cytotoxicity, chitosan-silver nanocomposites are perfect objects for antibacterial materials.

Fabrication and antibacterial activity of chitosan-silver nanocomposites

In the literature, there are many different routes of those antibacterial nanocomposites obtaining. Chitosan is used not only as a matrix for nanoparticles but also as a reducing and stabilizing agent in silver nanoparticles synthesis [4, 48÷50]. It is a perfect example of an environmental friendly synthesis of AgNPs (*green synthesis*). Silver ions are being coordinated by amino groups of polymeric chains in chitosan acidic solution. Ions reduction to metallic silver nanoparticles is coupled with chitosan hydroxyl groups oxidation [39, 51]. Due to the presence of chemical bond between AgNPs and chitosan chains, silver nanoparticles are strongly attached to the matrix [37]. The system creates polymeric chains network with embedded silver nanoparticles

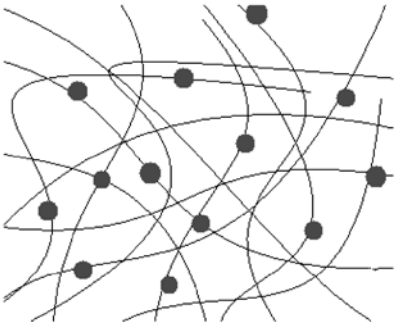

Fig. 2. Schematic figure of chitosans chains embedding and stabilizing reduced silver

Due to the permanent connection between AgNPs and polymeric matrix it is possible to omit a problem of nanoparticles aggregation or undesired modifications after contact with physiological fluids. [25]. Chitosan stabilization provides a long-term stability of materials.

Besides this particular case, there are many other AgNPs synthesis possibilities and further nanocomposites fabrication. As mentioned

before, there are other reducing agents for this purpose: sodium borohydride, polyvinylpyrrolidone (PVP), ascorbic acid, aniline or other than chitosan polysaccharides [4, 35, 39, 52÷55]. Taking into account minimization of toxicity, chitosan seems to be a perfect choice for a reducing and stabilizing agent and for the main component of the nanocomposites. Another important advantage of chitosan usage as a matrix is its bacteriostatic activity. Biocide activity of AgNPs in connection with bacteriostatic chitosan, increases chances of success in fighting down bacterial infections. Synergic antibacterial action of chitosan-silver nanocomposites has been proved [48]. In order to fully exploit antibacterial potential of those nanocomposites, AgNPs must be homogenously dispersed in a polymeric matrix (without forming huge aggregates). According to application, chitosan-silver nanocomposites occur in a different forms: colloids, powders or membranes [4, 50, 56].

Nanocomposites antibacterial activity examples

Obtained in our laboratory chitosan based silver nanoparticles and further nanocomposites in form of films met the requirements of potential medical application [57]. Homogenously and finely dispersed over the whole membrane AgNPs exhibited desired dimensions and their attachment in the matrix was strong enough to keep the metallic silver in the polymer without releasing it to the environment. Their high antibacterial activity coming from the biocide effect of AgNPs, silver ions and bacteriostatic chitosan was demonstrated against two antibiotic resistant, biofilm forming strains of *Staphylococcus aureus*

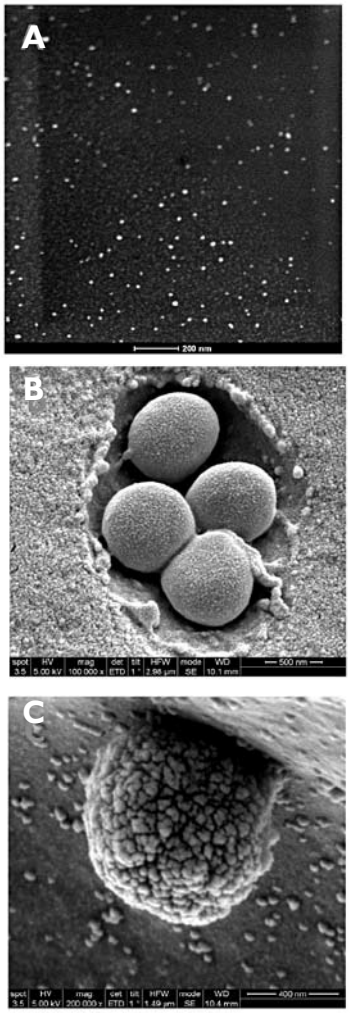

Fig. 3. (A) TEM picture of chitosan-silver nanocomposites executed in a dark-field mode, homogeneity of AgNPs dispersion in polymeric matrix is evident (bright points execute AgNPs); (B) *S. aureus* 9213 bacterial cells after 24 h of incubation with chitosan membrane; (C) *S. aureus* 9213 bacterial cells after 24 h of incubation with chitosan-silver nanocomposite. In contrast to pure chitosan membrane, nanocomposites with silver induced significant changes in the bacterial cell wall morphology, leading in consequence to cell death

Chitosan-silver nanocomposites exhibit a strong biocide effect also against many other strains as: *Escherichia coli, Escherichia bacillus, Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterococcus faecium, Candida albicans, Lactobacillus fermentum* [4, 39, 48, 49].

Summary

Chronic bacterial infections are a serious, worrisome problem, mainly because of increasing resistance of bacterial strains against antibiotics. Application of nanotechnology in creating new, effective medicines enables application of innovative solutions in fighting down pathogenic microorganism. Small dimensions of nanomaterials provide unique physicochemical and biological properties. Chitosan-silver nanocomposites are ideal alternative for ineffective antibiotics. They exhibit numerous advantages from medical applications point of view. Synergic antibacterial mechanism of chitosan and silver nanoparticles provides efficient bacterial infections control.

Literature

1. Fux C.A., Costerton J.W., Stewart P.S., Stoodley P.: *Survival strategies of infectious biofilms*. Trends in Microbiology 2005, **13**, (1), 34–40.
2. European Centre for Disease Prevention and Control/European Medicines Agency Joint Technical Report The bacterial challenge: time to react. http://www.ecdc.europa.eu/en/publications/Publications/0909_TER_The_Bacterial_Challenge_Time_to_React.pdf, 2009.
3. Dash M., Chiellini F., Ottenbrite R.M., Chiellini E.: *Chitosan – A versatile semi-synthetic polymer in biomedical applications*. Progress in Polymer Science 2011, **36**, (8), 981–1014.
4. Dongwei Wei W.S., Weiping Qian, Yongzhong Ye, Xiaoyuan Mac: *The synthesis of chitosan-based silver nanoparticles and their antibacterial activity*. Carbohydrate Research 2009, **344**, 2375–2382.
5. Raafat D., Sahl H.-G.: *Chitosan and its antimicrobial potential – a critical literature survey*. Microbial Biotechnology 2009, **2**, (2), 186–201.
6. Ralston G.B.T., M.V., Wrench P.M.: *Inhibition of fermentation in bakers yeast by chitosan*. Biochimica et Biophysica Acta 1964, **93**, (3), 653.
7. Fang S.W., Li C.F., Shih D.Y.C.: *Antifungal activity of chitosan and its preservative effect on low-sugar candied kumquat*. Journal of food protection 1994, **57**, (2), 136–140.
8. Ignatova M., Manolova N., Rashkov I.: *Novel antibacterial fibers of quaternized chitosan and poly(vinyl pyrrolidone) prepared by electrospinning*. European Polymer Journal 2007, **43**, (4), 1112–1122.
9. Takahashi T., Imai M., Suzuki I., Sawai J.: *Growth inhibitory effect on bacteria of chitosan membranes regulated with deacetylation degree*. Biochemical Engineering Journal 2008, **40**, (3), 485–491.
10. Varma A.J., Deshpande S.V., Kennedy J.F.: *Metal complexation by chitosan and its derivatives: a review*. Carbohydrate Polymers 2004, **55**, (1), 77–93.
11. Kong M., Chen X.G., Xing K., Park H.J.: *Antimicrobial properties of chitosan and mode of action: A state of the art review*. International Journal of Food Microbiology 2010, **144**, (1), 51–63.
12. Zheng L.-Y., Zhu J.-F.: *Study on antimicrobial activity of chitosan with different molecular weights*. Carbohydrate Polymers 2003, **54**, (4), 527–530.
13. Kofuji K., Akamine H., Qian C.J., Watanabe K., Togan Y., Nishimura M., Sugiyama I., Murata Y., Kawashima S.: *Therapeutic efficacy of sustained drug release from chitosan gel on local inflammation*. International Journal of Pharmaceutics 2004, **272**, 65–78.
14. Bhattarai N., Gunn J., Zhang M.: *Chitosan-based hydrogels for controlled, localized drug delivery*. Advanced Drug Delivery Reviews 2009, **62**, (1), 83–99.
15. Dudhani A.R., Kosaraju S.L.: *Bioadhesive chitosan nanoparticles: Preparation and characterization*. Carbohydrate Polymers 2010, **81**, (2), 243–251.

16. Ta H.T., Dass C.R., Dunstan D.E.: *Injectable chitosan hydrogels for localised cancer therapy*. Journal of Controlled Release 2008, **126**, (3), 205–216.
17. Prego C., Torres D., Fernandez-Megia E., Novoa-Carballal R., Qui E., Alonso M.J.: *Chitosan-PEG nanocapsules as new carriers for oral peptide delivery: Effect of chitosan pegylation degree*. Journal of Controlled Release 2006, **111**, (3), 299–308.
18. Illum L., Jabbal-Gill I., Hinchcliffe M., Fisher A.N., Davis S.S.: *Chitosan as a novel nasal delivery system for vaccines*. Advanced Drug Delivery Reviews 2001, **51**, 81–96.
19. Saranya N., Moorthi A., Saravanan S., Devi M.P., Selvamurugan N.: *Chitosan and its derivatives for gene delivery*. International Journal of Biological Macromolecule 2010, **48**, (2), 234–238.
20. Atiyeh B.S., Costagliola M., Hayek S.N., Dibo SA: *Effect of silver on burn wound infection control and healing: Review of the literature*. Burns 2007, **33**, (2), 139–148.
21. Bumgardner J.D., Wiser R., Gerard P.D., Bergin P., Chestnutt B., Marini M., Ramsey V., Elder S.H., Gilbert J.A.: *Chitosan: potential use as a bioactive coating for orthopaedic and craniofacial/dental implants*. Journal of Biomaterials Science, Polymer Edition 2003, **14**, (5), 423–438.
22. Radhakumary C., Nair P.D., Reghunadhan Nair C.P., Mathew S.: *Chitosan-graft-poly(vinyl acetate) for hemodialysis applications*. Journal of Applied Polymer Science 2012, **125**, (3), 2022–2033.
23. Wedmore I., McManus J.G., Pusateri A.E., Holcomb J.B.: *A special report on the chitosan-based hemostatic dressing: experience in current combat operations*. J Trauma 2006, **60**, (3), 655–658.
24. Vongchan P., Sajomsang W., Subyen D., Kongtawelert P.: *Anticoagulant activity of a sulfated chitosan*. Carbohydrate Research 2002, **337**, (13), 1239–1242.
25. Ravi Kumar M.N.V.: *A review of chitin and chitosan applications*. Reactive and Functional Polymers 2000, **46**, (1), 1–27.
26. Arora A., Padua G.W.: *Review: Nanocomposites in Food Packaging*. Journal of Food Science 2010, **75**, (1), R43-R49.
27. Kuo W.-S., Chang C.-N., Chang Y.-T., Yeh C.-S.: *Antimicrobial gold nanorods with dual-modality photodynamic inactivation and hyperthermia*. Chemical Communications 2009, (32), 4853–4855.
28. Kim J.S., Kuk E., Yu K.N., Kim J.-H., Park S.J., Lee H.J., Kim S.H., Park Y.K., Park Y.H., Hwang C.-Y., Kim Y.-K., Lee Y.-S., Jeong D.H., Cho M.-H.: *Antimicrobial effects of silver nanoparticles*. Nanomedicine: Nanotechnology, Biology and Medicine 2007, **3**, (1), 95–101.
29. Cioffi N., Torsi L., Ditaranto N., Tantillo G., Ghibelli L., Sabbatini L., Bleve-Zacheo T., D'Alessio M., Zambonin P.G., Traversa E.: *Copper Nanoparticle/Polymer Composites with Antifungal and Bacteriostatic Properties*. Chemistry of Materials 2005, **17**, (21), 5255–5262.
30. Ülkür E., Oncul O., Karagoz H., Yeniz E., Çeliköz B.: *Comparison of silver-coated dressing (Acticoat™), chlorhexidine acetate 0.5% (Bactigrass®), and fusidic acid 2% (Fucidin®) for topical antibacterial effect in methicillin-resistant Staphylococci-contaminated, full-skin thickness rat burn wounds*. Burns 2005, **31**, (7), 874–877.
31. Vaidyanathan R., Kalishwaralal K., Gopalram S., Gurunathan S.: *Nanosilver – The burgeoning therapeutic molecule and its green synthesis*. Biotechnology Advances 2009, **27**, (6), 924–937.
32. Panáček A., Kolář M., Večeřová R., Prucek R., Soukupová J., Kryštof V., Hamal P., Zbořil R., Kvítek L.: *Antifungal activity of silver nanoparticles against Candida spp*. Biomaterials 2009, **30**, (31), 6333–6340.
33. Kholoud M.M., Abou El-Nour, Eftaiha A.A., Al-Warthan A., Ammar R.A-.A.: *Synthesis and applications of silver nanoparticles*. Arabian Journal of Chemistry 2010, **3**, (3), 135–140.
34. Sharma V.K., Yngard R.A., Lin Y.: *Silver nanoparticles: Green synthesis and their antimicrobial activities*. Advances in Colloid and Interface Science 2009, **145**, 83–96.
35. Qin Y., Ji X., Jing J., Liu H., Wu H., Yang W.: *Size control over spherical silver nanoparticles by ascorbic acid reduction*. Colloids and Surfaces A: Physicochemical and Engineering Aspects 2010, **372**, 172–176.
36. Rai M., Yadav A., Gade A.: *Silver nanoparticles as a new generation of antimicrobials*. Biotechnology Advances 2009, **27**, (1), 76–83.
37. Sondi I., Salopek-Sondi B.: *Silver nanoparticles as antimicrobial agent: a case study on E. coli as a model for Gram-negative bacteria*. Journal of Colloid and Interface Science 2004, **275**, (1), 177–182.
38. Tran H.V., Tran L.D., Ba C.T., Vu H.D., Nguyen T.N., Pham D.G., Nguyen P.X.: *Synthesis, characterization, antibacterial and antiproliferative activities of monodisperse chitosan – based silver nanoparticles*. Colloids and Surfaces A: Physicochemical and Engineering Aspects 2010, **360**, 32–40.
39. Somnath Ghosh T.K.R. and Vasan H.N.: *Study of Antibacterial Efficacy of Hybrid Chitosan-Silver Nanoparticles for Prevention of Specific Biofilm and Water Purification*. In 2011; Vol. 2011.
40. Lewinski N., Colvin V., Drezek R.: *Cytotoxicity of Nanoparticles*. Small 2008, **4**, (1), 26–49.
41. Chi Z., Liu R., Zhao L., Qin P., Pan X., Sun F., Hao X.: *A new strategy to probe the genotoxicity of silver nanoparticles combined with cetylpyridine bromide*. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2009, **72**, (3), 577–581.
42. Foldbjerg R., Dang D., Autrup H.: *Cytotoxicity and genotoxicity of silver nanoparticles in the human lung cancer cell line, A549*. Archives of Toxicology 2011, **85**, (7), 743–750.
43. Kim S., Choi J.E., Choi J., Chung K.-H., Park K., Yi J., Ryu D.-Y.: *Oxidative stress-dependent toxicity of silver nanoparticles in human hepatoma cells*. Toxicology in Vitro 2009, **23**, (6), 1076–1084.
44. http://www.washingtonpost.com/wp-dyn/content/article/2006/11/22/AR2006112201979.html, 2013.
45. Choi Y.-J., Luo T.-J.M.: *Self-Assembly of Silver-Aminosilica Nanocomposites through Silver Nanoparticle Fusion on Hydrophobic Surfaces*. ACS Applied Materials & Interfaces 2009, **1**, (12), 2778–2784.
46. Levin C.S., Hofmann C., Ali T.A., Kelly A.T., Morosan E., Nordlander P., Whitmire K.H., Halas N.J.: *Magnetic-Plasmonic Core-Shell Nanoparticles*. ACS Nano 2009, **3**, (6), 1379–1388.
47. Dallas P., Sharma V.K., Zboril R.: *Silver polymeric nanocomposites as advanced antimicrobial agents: Classification, synthetic paths, applications, and perspectives*. Advances in Colloid and Interface Science 2010, **166**, 119–135.
48. Potara M.E.J., Damert A., Popescu O., Canpean V. and Astilean S: *Synergistic antibacterial activity of chitosan–silver nanocomposites on Staphylococcus aureus*. Nanotechnology 2011, **22**, (13), 135101.
49. Vimala K., Mohan Y.M., Sivudu K.S., Varaprasad K., Ravindra S., Reddy N.N., Padma Y., Sreedhar B., MohanaRaju K.: *Fabrication of porous chitosan films impregnated with silver nanoparticles: A facile approach for superior antibacterial application*. Colloids and Surfaces B: Biointerfaces 2009, **76**, (1), 248–258.
50. Thomas V., Yallapu M.M., Sreedhar B., Bajpai S.K.: *Fabrication, Characterization of Chitosan/Nanosilver Film and Its Potential Antibacterial Application*. Journal of Biomaterials Science, Polymer Edition 2009, **20**, (14), 2129–2144.
51. Wei D., Qian W.: *Facile synthesis of Ag and Au nanoparticles utilizing chitosan as a mediator agent*. Colloids and Surfaces B: Biointerfaces 2008, **62**, (1), 136–142.
52. Wani I.A., Ganguly A., Ahmed J., Ahmad T.: *Silver nanoparticles: Ultrasonic wave assisted synthesis, optical characterization and surface area studies*. Materials Letters 2011, **65**, (3), 520–522.
53. Kim J.-S.: *Reduction of Silver Nitrate in Ethanol by Poly(N-vinylpyrrolidone)*. J. Ind. Eng. Chem. 2007, **13**, (4), 566–570.
54. Huang H., Yang X.: *Synthesis of polysaccharide-stabilized gold and silver nanoparticles: a green method*. Carbohydrate Research 2004, **339**, (15), 2627–2631.
55. Tan Y., Li Y., Zhu D.: *Preparation of silver nanocrystals in the presence of aniline*. Journal of Colloid and Interface Science 2003, **258**, (2), 244–251.
56. Twu Y.-K., Chen Y.-W., Shih C.-M.: *Preparation of silver nanoparticles using chitosan suspensions*. Powder Technology 2008, **185**, (3), 251–257.
57. Regiel A., Irusta S., Kyzioł A., Arruebo M., Santamaria J.: *Preparation and characterization of chitosan-silver nanocomposite films and their antibacterial activity against Staphylococcus aureus*. Nanotechnology 2013, **24**, (1), 015101.

Anna REGIEL – M.Sc., graduated from the Faculty of Chemistry of the Jagiellonian University in Krakow (2012). Now she continues PhD studies in the Coordination and Bioinorganic Physicochemistry Group at the Faculty of Chemistry UJ. Her main scientific interest focuses on various nanomaterials exhibiting antibacterial activity for medical application.

e-mail:regiel@chemia.uj.edu.pl; phone: + 48 12 663 22 21

Agnieszka KYZIOŁ – Ph.D., graduated from the Faculty of Chemistry of the Jagiellonian University (2002). In 2007she received her PhD degree in Chemistry. She is currently an assistant professor in the Coordination and Bioinorganic Physicochemistry Group at the Faculty of Chemistry UJ. Her main interests and research work are focused on metal complexes and biomaterials with potential biological activity for medical applications (anticancer therapies, antimicrobial agents). She is co-author of over 20 scientific publications and numerous conference presentations.

e-mail: kyziol@chemia.uj.edu.pl; phone: + 48 12 663 22 21

Manuel ARRUEBO – Professor, promoted in 2012 from Assistant Professor to Associate Professor in Chemical Engineering at the University of Zaragoza, Spain. He is the author of 50 scientific peer review papers some of them having a high-impact factor such as Nature Nanotechnology, Nano Today. He has been invited to write several review papers (i.e., Wiley Interdisciplinary Review in Nanomedicine and Nanobiotechnology, Expert Opinion on Drug Delivery, etc.) He is co-author of 6 patents issued to the University of Zaragoza and to several industrial partners, also co-author of three chapters in scientific books (one of them a Handbook). He has worked as a postdoctoral researcher at the Massachusetts Institute of Technology under the supervision of Professor Robert S. Langer. He has been awarded with one laboratory to carry out independent research in the Aragon Biomedical Research Center (CIBA).

e-mail: arruebom@unizar.es

Nanosafety 2013

Nov. 20-22, 2013

Saarbrücken, Germany

Nanotechnologies are developing with increasing pace. They impact a broad range of industrial sectors, from energy, optics, electronics to food and biomedicine. Using these technologies, materials, objects, and structures in the size range between 1-100 nanometres are generated, manipulated or analysed. For a sustainable development of these promising technologies, aspects of nanosafety gain more and more importance.

Nanosafety includes:

– a detailed knowledge on the materials as well as acquisition of their properties
– elucidation of the effects of nanomaterials on human beings, including detailed analyses on their mode of action and structure activity relationships
– assessment of the impact of nanomaterials on living organisms and the environment
– the detection, identification, and quantification of nanomaterials in complex matrices, for example cells and tissues as well as standardization, legislative, regulatory and social aspects.

http://nanosafety.inm-gmbh.de/

Fertilizer Outlook and Technology Conference

Nov. 19-21, 2013

Tampa Marriott Waterside Hotel and Marina

Tampa, Fla.

The Fertilizer Institute (TFI) and the Fertilizer Industry Round Table (FIRT) jointly host the Fertilizer Outlook and Technology Conference in the fall of each year. The conference is geared towards industry members, financial analysts, business consultants, trade press representatives, agricultural retailers, agronomists, engineers and government economists. Conference participants can expect to gain perspective on the outlook for agriculture and major fertilizer materials and inputs from industry experts. New technology and issues that impact plant nutrition are also key topics of discussion at the conference. The 2013 Fertilizer Outlook and Technology Conference will take place Nov. 19-21 in Tampa, Fla., at the Tampas Marriott Waterside Hotel.

Industry experts present the supply and demand factors affecting the markets for agriculture, N, P and K, and sulfur, and discuss issues of relevance such as the factors driving food prices and new technologies. They also address technical issues relevant to improving fertilizer products, manufacturing, and distribution methods.

http://www.firt.org/