Proc. of the International Conference on Mechanochemistry and Mechanical Alloying, Kraków, Poland, June 22–26, 2014

Mechanochemistry of Solids: New Prospects for Extractive Metallurgy, Materials Science and Medicine

P. Baláž*, M. Baláž, M. Achimovičová, Z. Bujňáková and E. Dutková
Institute of Geotechnics, Slovak Academy of Sciences, Watsonova 45, Košice, Slovakia

In this review paper recent advances in chalcogene mechanochemistry are described. Three selected areas are being covered, i.e. metallurgy, materials science, and medicine. In extractive metallurgy, the processing of copper arsenic mineral enargite (Cu_3AsS_4) with the aim of its dearsenification and subsequent preparation of a new anticancer drug (Na_3AsS_4) and of copper in nanocrystalline state ($\approx$ 20 nm) illustrate the non-traditional prospect of ore treatment. In material science, the new nanocrystalline semiconductors were synthesized mechanochemically, e.g. selenides of zinc and lead (ZnSe, PbSe) and bismuth sulphide (Bi_2S_3). Metal and chalcogene were applied as reaction precursors. In some cases, the amino acids (cystine, cysteine) were applied as sulphur precursor, in order to provide reactive sites on synthesized solid (PbS) for bioconjugation and to prevent agglomeration. The concept of nanomilling is described as a way to prepare effective substances for cancer treatment in medicine. *In vitro* activity of realgar (As_4S_4) as an example is described. In all three areas the focus is aimed also on industrial applications where suitable large-scale mills are described. The described examples represent the contemporary aim of mechanochemists — to prepare substances with the desired properties in a reproducible way under easy-operating, environmentally friendly and essentially waste-free conditions.

DOI: 10.12693/APhysPolA.126.879
PACS: 81.05.Dz, 81.20.Wk, 81.07.Bc

1. Introduction

Ostwald, one of the founders of mechanochemistry, regarded it as a part of physical chemistry at the same level as thermochemistry, electrochemistry and photochemistry [1]. However, from his times the great expansion of mechanochemistry into various fields has been documented [2]. Nowadays, mechanochemistry is very well-accepted as a discipline and number of dedicated sessions in the international events can be recognized [3]. In the period between the previous INCOME conference in Herceg Novi (2011) and the conference held in Krakow (2014), the important achievements in the field have been reached. Among others, the comprehensive reviews on mechanochemistry have been published, where the exceptionality of various milling modes and new applications can be well-traced [2, 4–16]. The aim of this review paper is to illustrate the recent impacts on such fields like extractive metallurgy, materials science, and medicine.

2. Extractive metallurgy

According to classical view, extractive metallurgy is the art and science of extracting metals from their ores by chemical methods [17]. It is divided into three subdisciplines: hydrometallurgy, pyrometallurgy and electrometallurgy. The most convincing intervention of mechanochemistry into metallurgical operations has been obtained in hydrometallurgy [18, 19], which is science and technology of extracting metals from minerals by using aqueous/non-aqueous solutions.

Recently, the multistep metallurgical process including mechanochemical steps for the treatment of enargite concentrate has been developed [20]. Enargite (Cu_3AsS_4) prevails among copper-bearing minerals with high Cu content, but it is combined, unfortunately, with high As content. There are several hydrometallurgical options to treat enargite including acid leaching, ammonia leaching and bio-leaching. However, the most effective solution for selective removal of As from enargite seems to be alkaline leaching [21–23]. In combination with mechanochemistry, the effective process can be developed as illustrated by Fig. 1, where the simplified flowchart with five steps of treatment is depicted.

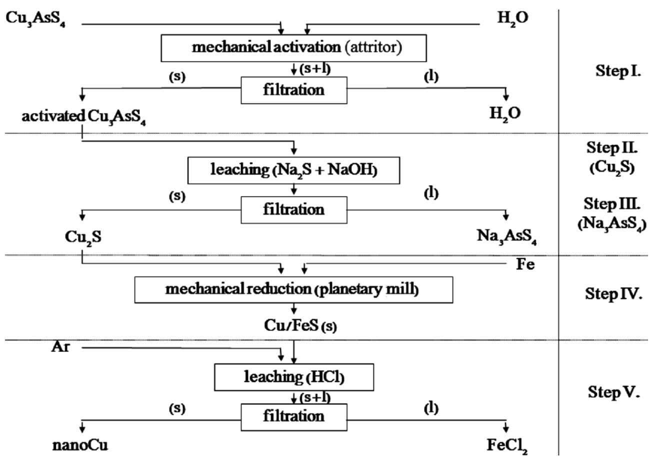

Fig. 1. Multistep process of enargite treatment with intervention of mechanochemistry [20].

Finally, nanocopper and sodium thioarsenate Na_3AsS_4 as potential anticancer drug can be obtained from enargite mineral [20]. This treatment typically illustrates the principal possibility of transforming minerals to products with advanced applications.

*corresponding author; e-mail: balaz@saske.sk

3. Materials science

Semiconductor materials with reduced dimensions have shown to exhibit electronic and optical properties which vary with size of particles, thus making them potential candidates for applications involving tunability of optical and/or electronic properties [24, 25]. In the case of semiconductor nanocrystals, also called quantum dots, basically novel properties of the matter, generally described as "size-quantification effects" can be studied due to the large number of surface atoms and/or the three-dimensional confinement of electrons [26]. The new ways of synthesis, e.g. mechanochemical one [8, 10, 19, 27, 28], represent a challenge in the preparation of such compounds.

3.1. Mechanochemical synthesis of chalcogenides from elements

Chalcogenides exhibit a great variety of physical, chemical and physico-chemical properties. They display similar structural defects to oxides with cation vacancies, interstitial cations or anionic defects. During the last few years, the synthesis and characterization of new chalcogenide compounds have received considerable attention. Mechanochemical synthesis has been applied for preparation of a wide range of chalcogenide nanocrystals [10, 18, 29–43].

As latest examples the mechanochemical synthesis of clausthalite (lead selenide PbSe) and bismuthine (bismuth sulphide Bi_2S_3) can be given [37, 44]. In the first case (Fig. 2), the product was prepared in an industrial eccentric vibratory mill (milling time is given in the figure).

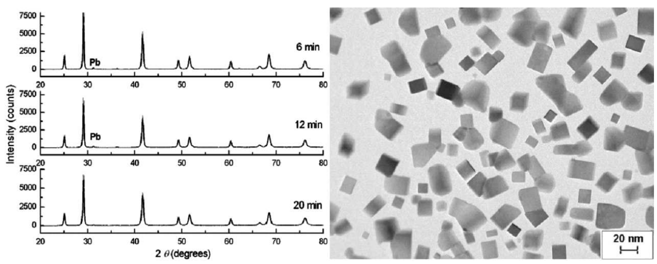

Fig. 2. Mechanochemical synthesis of PbSe: XRD patterns (left), TEM images (right) [37].

Degree of conversion to PbSe was 97% after 6 min of treatment and the cubic particles ~20 nm (depending on milling time) were obtained. The preparation of Bi_2S_3 was also straightforward as illustrated by Fig. 3.

The conversion to Bi_2S_3 was total after 60 min of milling in a laboratory planetary mill. The prepared semiconductor nanocrystals belong to orthorhombic phase with the crystallite size of about 26 nm. The comprehensive description of the synthesis process was given by the study of structural, surface, optical, and thermal properties as well as the kinetics of Bi_2S_3 formation [44, 45].

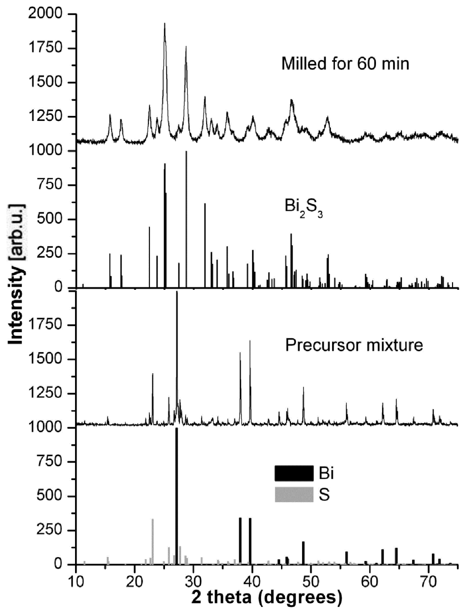

Fig. 3. Mechanochemical synthesis of Bi_2S_3: XRD patterns [44].

3.2. Mechanochemical synthesis of sulphides from organic salts and aminoacids

The preparation of lead sulphide PbS from lead acetate $(CH_3COO)_2Pb{\cdot}3H_2O$ and L-cystine $C_6H_{12}N_2O_4S_2$ has been reported recently [46]. The morphology of the synthesized PbS nanocrystals is documented by Fig. 4.

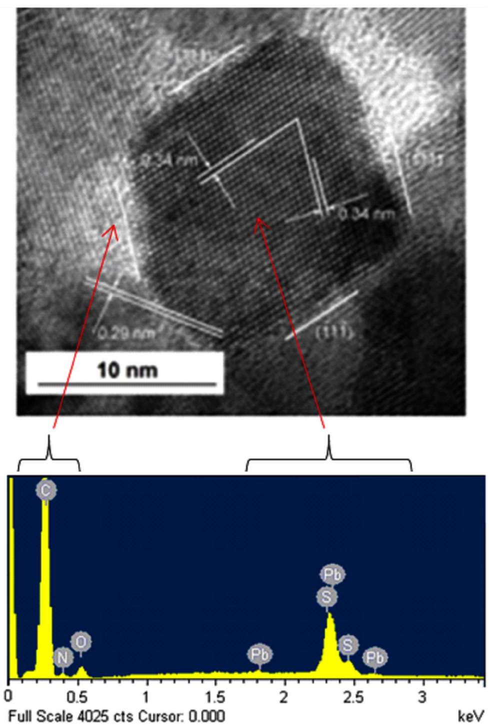

Fig. 4. HRTEM image of PbS nanocrystal (top) and corresponding EDS spectrum (bottom); modified from [46].

The PbS was formed in a rhombic shape exhibiting faceting along {111}planes. The nanocrystal exhibited a high crystallinity without any crystal defects. The energy dispersive spectrum EDS in Fig. 4 unambiguously confirms that there is cystine in the sample, because elements C, N, O, and S are present. Moreover, the presence of Pb indicates that the PbS nanoparticles are wrapped by cystine as confirmed by light spots in high resolution transmission electron microscopy (HRTEM) image given in Fig. 4. It was shown that the amino acid L-cystine has a dual role: (1) acting as a source of sulphur for the mechanochemical synthesis, and (2) binding to the synthesized PbS, which makes it possible for the nanoparticles to be biofunctionalized for medical purposes.

In paper [47] the successful synthesis of PbS nanocrystals has been reported by co-milling lead acetate with the eggshell membrane (ESM). ESM represents perspective biomaterial [48] composed mainly of proteins, which consist of various amino acids. Among them, also sulphur-containing ones are present. As a result, PbS nanocrystals with crystallite sizes ~8 nm were produced. SEM images illustrating the course of the synthesis are given in Fig. 5.

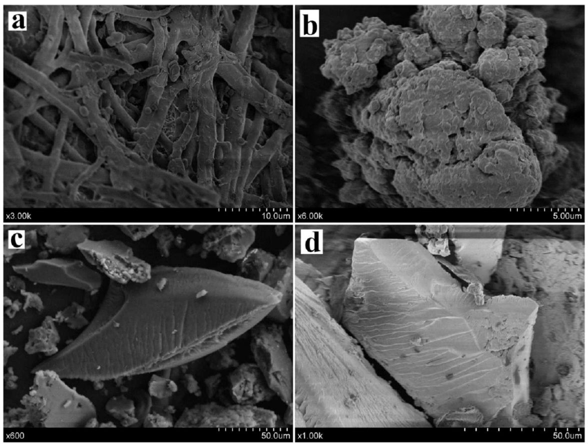

Fig. 5. SEM images of (a) pure ESM and the reaction mixture milled for: (b) 60 min, (c) 120 min, and (d) 180 min [47].

The progress of the mechanochemical synthesis can be clearly seen. During the milling the originally fibrous structure of ESM (Fig. 5a) is almost completely destructed and large amorphous clamps with the residues of fibers can be seen (Fig. 5b). After supplying the additional milling energy, the particles of PbS with an exotic morphology are formed (Fig. 5c,d). The fibrous structure of ESM has completely disappeared and its residue became part of the product. The presence of lead sulphide was confirmed by X-ray diffraction (XRD) and EDS analysis.

4. Medicine

While significant progress in the treatment of many diseases has been made, cancer is still the second leading cause of death in the world. Therefore, the search for new anticancer drugs still remains a real issue. Nanomilling [4, 49–52] represents a mechanochemical approach for producing nanoparticles, which can effectively target tumor tissue, as well as play an important role in prevention and diagnosis of the disease.

Arsenic compounds had a long Janus-type interaction with humanity. On the one hand, they have been extensively utilized, but on the other hand, their poisonous properties have caused misery and many deaths. However, arsenic substances have also been known to have a therapeutic effect and several reviews have been published on this topic [53–58]. Mechanochemical preparation and anticancer effects of arsenic sulphide As_4S_4 (realgar) nanoparticles have been clearly demonstrated in several papers [59–64]. The increase in surface area and the shift of particle size to nanoregion had positive effect on improved dissolution disorder of cell membrane and reduced viability of various cancer cell lines. For illustration, the comparison of selected nanomilled As_4S_4 particles with approved anticancer drug As_2O_3 (ATO, brand name TRISENOX^{TM}) is shown in Fig. 6.

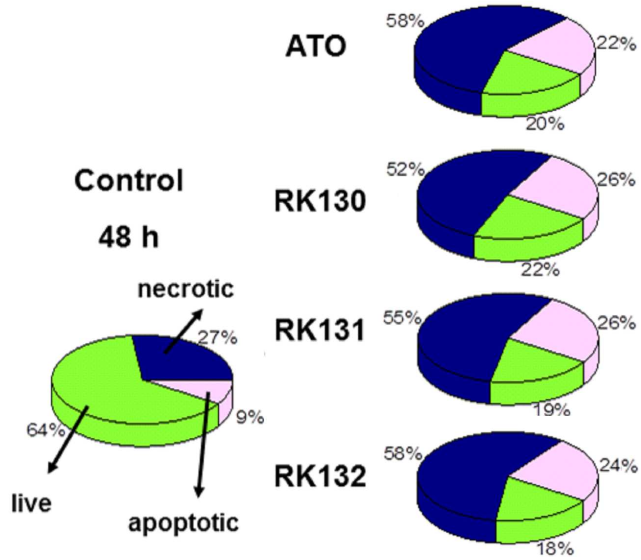

Fig. 6. Comparison of biological activity of As_4S_4 nanoparticles (RK130–RK132) with arsenic oxide As_2O_3 (ATO): RK130 — chemical (Sigma Aldrich), RK131 — mineral realgar, RK132 — mineral pararealgar.

The less toxic As_4S_4 nanoparticles exhibit practically the same distribution of live, necrotic and apoptotic cells as highly toxic ATO. Moreover, IC_{50} values (the concentration of a drug that is required for 50% inhibition of the proliferation of selected cancer cells) favour As_4S_4 (0.031–0.033 μg mL^{-1}) over ATO (0.050 μg mL^{-1}). It follows that for the same anticancer activity, less arsenic drug is needed. These effects obtained for *in vitro* experiments open a lot of new challenges for *in vivo* treatment of cancer.

5. Industrial aspects

Mechanochemistry offers innovative procedures in which the improvement in technological processes governed by their application can be attained via a contribution of several effects which influence the properties of processed solids. The main advantages are the decrease in the number of technological stages, the exclusion of operations that involve the use of gases and the high temperatures and working under environmentally friendly conditions. The key aspect is the proper selection of a mill, which can serve as a mechanochemical reactor. Different types of mills suitable for the large-quantity production can be used [19]. As an example, which is in accordance with the topic of this paper, several types are shown in Fig.7.

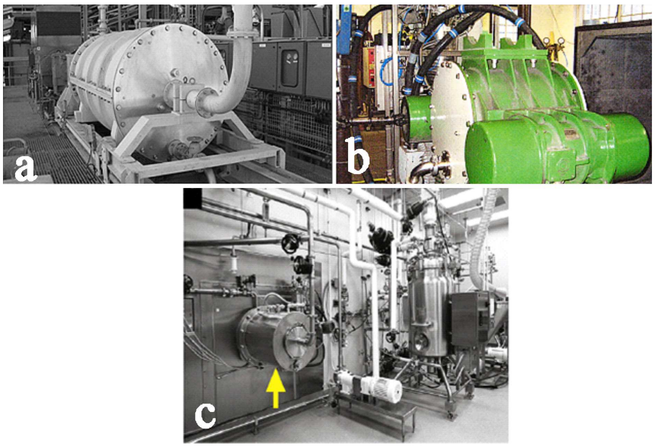

Fig. 7. Industrial mills used for applications in (a) extractive metallurgy: stirred ball mill [19], (b) materials science: eccentric vibratory mill [65] and (c) pharmaceutical industry: stirred ball mill (the milling chamber of the large-scale mill is marked with the arrow) [4].

6. Conclusions

After successful application to processing of minerals, mechanochemistry is heading for new fields of study such as preparation of nanocrystalline substances and nanodrugs [10]. In this review, updated information from the field of extractive metallurgy, materials science, and medicine is provided.

Acknowledgments

The authors gratefully acknowledge the support of APVV grant (VV-0189-10) and VEGA grants (2/0027/14, 2/0051/14).

References

[1] W. Ostwald, *Handbuch der Allgemeinen Chemie*, Akademische Verlagesellschaft, Leipzig 1919.

[2] E. Boldyreva, *Chem. Soc. Rev.* **42**, 7719 (2013).

[3] M. Senna, in: *Proc. VIIIth Int. Conf. on Mechanochemistry and Mechanical Alloying, Kraków*, Eds: K. Wieczorek-Ciurowa, D. Oleszak, Cracow University of Technology, Cracow 2014, p. 3.

[4] E. Merisko-Liversidge, G.G. Liversidge, *Adv. Drug Del. Rev.* **63**, 427 (2011).

[5] A. Stolle, T. Szuppa, S.E.S. Leonhardt, B. Ondruschka, *Chem. Soc. Rev.* **40**, 2317 (2011).

[6] V. Šepelák, K.D. Becker, *J. Korean Ceram. Soc.* **42**, 19 (2012).

[7] P. Billik, M. Čaplovičová, in: *Advances in Nanotechnology*, Eds. Z. Barul, Z. Trenor, Nova Publ., New York 2012.

[8] S.L. James, C.J. Adams, C. Bolm, D. Braga, P. Collier, T. Friščić, F. Grepioni, K.D.M. Harris, G. Hyett, W. Jones, A. Krebs, J. Mack, L. Maini, A.G. Orpen, I.P. Parkin, W.C.'Shearouse, J.W. Steed, D.C. Waddell, *Chem. Soc. Rev.* **41**, 413 (2012).

[9] A. Nasser, U. Mingelgrin, *Appl. Clay Sci.* **67-68**, 141 (2012).

[10] P. Baláž, M. Achimovičová, M. Baláž, P. Billik, Z. Cherkezova-Zheleva, J.M. Criado, F. Delogu, E. Dutková, E. Gaffet, F.J. Gotor, R. Kumar, I. Mitov, T. Rojac, M. Senna, A. Streletskii, K. Wieczorek-Ciurowa, *Chem. Soc. Rev.* **42**, 7571 (2013).

[11] C.L. Zhang, J.W. Wang, J.F. Bai, J. Guan, W.J. Wu, C.X. Guo, *Waste Manage. Res.* **31**, 759 (2013).

[12] V. Šepelák, A. Düvel, M. Wilkening, K.D. Becker, P. Heitjans, *Chem. Soc. Rev.* **42**, 7507 (2013).

[13] S.E. Zhu, F. Li, G.W. Wang, *Chem. Soc. Rev.* **42**, 7535 (2013).

[14] G.W. Wang, *Chem. Soc. Rev.* **42**, 7668 (2013).

[15] K. Ralphs, C. Hardacre, S.L. James, *Chem. Soc. Rev.* **42**, 7701 (2013).

[16] P. Baláž, M. Baláž, Z. Bujňáková, *Chem. Eng. Technol.* **37**, 747 (2014).

[17] F. Habashi, *A Textbook of Hydrometallurgy*, Metallurgie Extractive Quebec, Sainte Foy, Quebec 1993.

[18] P. Baláž, *Extractive Metallurgy of Activated Minerals*, Elsevier, Amsterdam 2000.

[19] P. Baláž, *Mechanochemistry in Nanoscience and Minerals Engineering*, Springer, Berlin 2008.

[20] Z. Bujňáková, P. Baláž, A. Zorkovská, *Int. J. Miner. Proc.* **127**, 28 (2014).

[21] D. Filippou, P. St-Germain, T. Grammatikopoulos, *Miner. Process. Extr. Metall. Rev.* **28**, 247 (2007).

[22] M.S. Safarzadeh, M.S. Moats, J.D. Miller, *Miner. Process. Extr. Metall. Rev.* **35**, 283 (2014).

[23] M.S. Safarzadeh, M.S. Moats, J.D. Miller, *Miner. Process. Extr. Metall. Rev.* **35**, 390 (2014).

[24] L. Brus, *J. Quantum Electron.* **22**, 1909 (1986).

[25] S.B. Qadri, J. Yang, B.R. Ratna, E.F. Skelton, J.Z. Hu, *Appl. Phys. Lett.* **69**, 2205 (1996).

[26] P.D. Yang, C.M. Lieber, *Science* **273**, 1836 (1996).

[27] *Experimental and Theoretical Studies in Modern Mechanochemistry*, Eds. F. Delogu, G. Mulas, Transworld Research Network, Kerala 2010.

[28] T. Friščić, *J. Mater. Chem.* **20**, 7599 (2010).

[29] P. Baláž, T. Havlík, Z. Bastl, J. Briančin, *J. Mater. Sci. Lett.* **14**, 344 (1995).

[30] P. Baláž, T. Havlík, J. Briančin, R. Kammel, *Scr. Metall. Mater.* **32**, 1357 (1995).

[31] P. Baláž, T. Havlík, Z. Bastl, J.'Briančin, R. Kammel, *J. Mater. Sci. Lett.* **15**, 1161 (1996).

[32] P. Baláž, M. Bálintová, Z. Bastl, J. Briančin, V. Šepelák, *Solid State Ion.* **101**, 45 (1997).

[33] P. Baláž, T. Ohtani, *Mater. Sci. Forum* **343-346**, 389 (2000).

[34] P. Baláž, E. Boldižárová, E. Godočíková, J. Briančin, *Mater. Lett.* **57**, 1585 (2003).

[35] E. Godočíková, P. Baláž, E. Gock, *Acta Metall. Slov.* **10**, 73 (2004).

[36] P. Baláž, E. Boldižárová, E. Godočíková, *Mater. Sci. Forum* **480-481**, 453 (2005).

[37] M. Achimovičová, P. Baláž, J. Ďurišin, N. Daneu, J. Kováč, A. Šatka, A. Feldhoff, E. Gock, *Int. J. Mater. Res.* **102**, 441 (2011).

[38] M. Achimovičová, P. Baláž, T. Ohtani, N. Kostova, G. Tyuliev, A. Feldhoff, V. Šepelák, *Solid State Ion.* **192**, 632 (2011).

[39] M. Achimovičová, N. Daneu, A. Recnik, J. Ďurišin, P. Baláž, M. Fabián, J. Kováč, A. Šatka, *Chem. Pap.* **63**, 562 (2009).

[40] M. Achimovičová, A. Recnik, M. Fabián, P. Baláž, *Acta Montan. Slov.* **16**, 123 (2011).

[41] M. Achimovičová, P. Baláž, E. Dutková, E. Gock, V. Šepelák, *J. Balk. Tribol. Assoc.* **15**, 79 (2009).

[42] M. Achimovičová, K.L. da Silva, N. Daneu, A. Recnik, S. Indris, H. Hain, M. Scheuermann, H. Hahn, V. Šepelák, *J. Mater. Chem.* **21**, 5873 (2011).

[43] M. Achimovičová, F.J. Gotor, C.'Real, N. Daneu, *J. Mater. Sci.-Mater. Electron.* **23**, 1844 (2012).

[44] E. Dutková, L. Takacs, M.J. Sayagués, P. Baláž, J. Kováč, A. Šatka, *Chem. Eng. Sci.* **85**, 25 (2013).

[45] E. Dutková, M.J. Sayagués, A. Zorkovská, C. Real, P. Baláž, A. Šatka, J. Kováč, *Mater. Sci. Semicond. Proc.* **27**, 267 (2014).

[46] P. Baláž, M. Baláž, M. Čaplovičová, A. Zorkovská, Ľ. Čaplovič, M. Psotka, *Faraday Discuss.*, in press, 2014.

[47] M. Baláž, P. Baláž, M.J. Sayagués, A. Zorkovská, *Mater. Sci. Semicond. Proc.* **16**, 1899 (2013).

[48] M. Baláž, *Acta Biomater.* **10**, 3827 (2014).

[49] E. Merisko-Liversidge, G.G. Liversidge, E.R. Cooper, *Eur. J. Pharm. Sci.* **18**, 113 (2003).

[50] J.U.A.H. Junghanns, R.H. Muller, *Int. J. Nanomed.* **3**, 295 (2008).

[51] L. Peltonen, J. Hirvonen, *J. Pharm. Pharmacol.* **62**, 1569 (2010).

[52] M. Juhnke, E. John, *Chem. Eng. Technol.* **35**, 1931 (2012).

[53] Z.Y. Wang, *Cancer Chemother. Pharmacol.* **48**, S72 (2001).

[54] W.Z. Zhao, X. Lu, Y. Yuan, C.S. Liu, B.C. Yang, H. Hong, G.Y. Wang, F.Y. Zeng, *Int. J. Nanomed.* **6**, 1569 (2011).

[55] S.J. Ou, X.C. Shen, T. Jin, J. Xie, Y.F. Guo, *Front. Mater. Sci. China* **4**, 339 (2010).

[56] J. Liu, Y.F. Lu, Q. Wu, R.A. Goyer, M.P. Waalkes, *J. Pharmacol. Exp. Ther.* **326**, 363 (2008).

[57] P. Baláž, J. Sedlák, *Toxins* **2**, 1568 (2010).

[58] P.J. Dilda, P.J. Hogg, *Cancer Treat. Rev.* **33**, 542 (2007).

[59] J.Z. Wu, P.C. Ho, *Eur. J. Pharm. Sci.* **29**, 35 (2006).

[60] P. Baláž, M. Fabián, M. Pastorek, D. Cholujová, J. Sedlák, *Mater. Lett.* **63**, 1542 (2009).

[61] P. Baláž, A.V. Nguyen, M. Fabián, D. Cholujová, M. Pastorek, J. Sedlák, Z. Bujňáková, *Powder Technol.* **211**, 232 (2011).

[62] P. Baláž, J. Sedlák, M. Pastorek, D. Cholujová, K. Vignarooban, S. Bhosle, P. Boolchand, Z. Bujňáková, E. Dutková, O. Kartachova, B. Stalder, *J. Nano Res.* **18-19**, 149 (2012).

[63] P. Baláž, Z. Bujňáková, O. Kartachova, M. Fabián, B. Stalder, *Mater. Lett.* **104**, 84 (2013).

[64] Y. Tian, X.B. Wang, R.G. Xi, W. Pan, S. Jiang, Z. Li, Y. Zhaou, G.C. Gao, D. Liu, *Int. J. Nanomed.* **9**, 745 (2014).

[65] E. Gock, K.E. Kurrer, *Powder Technol.* **105**, 302 (1999).