Sjournals
Scientific Journal of Medical Science (2014) 3(2) 292-300
ISSN 2322-5025
doi: 10.14196/sjms.v3.i2.1127

Contents lists available at Sjournals
Scientific Journal of Medical Science
Journal homepage: www.Sjournals.com

Review article

Advances in biomaterials, new strategies, development and applications for biomedicine and engineering

S. Jebahi[a,*], , H. Oudadesse[a], E. Abdelfatteh[c], E. Hafedh[b], K. Hassib[d]

[a]*University of Rennes 1, UMR CNRS 6226, Campus de Beaulieu, 263 av. du Général Leclerc, 35042 Rennes, France.*
[b]*Animal Ecophysiology Laboratory, Sfax Faculty of Science, Department of Life Sciences ,Sfax ,Tunisia .*
[c]*Science Materials and Environement laboratory, Sfax Faculty of Science , Sfax, Tunisia.*
[d]*Histology , Orthopaedic and Traumatology laboratory Sfax Faculty of Medicine Sfax, Tunisia.*

*Corresponding author; University of Rennes 1, UMR CNRS 6226, Campus de Beaulieu, 263 av. du Général Leclerc, 35042 Rennes, France.

ARTICLE INFO

Article history,
Received 09 January 2014
Accepted 25 January 2014
Available online 28 Febreuary 2014

Keywords,
Tissue engineering
Therapeutic strategies
Factor growth
Nanotechnology
Gene delivery

ABSTRACT

One of the most exciting and rewarding research areas of materials science involves the applications to health care, especially to skeletal repair and reconstructive surgery. The potential benefits of these materials for this clinical needs, strongly depend on more research works and multidisciplinary approaches that combine engineering, and the technical expertise of medical specialists. The development regarding the tissue engineering and the social obligations to provide a better quality of life seemed to be the crucial factors to this progress . In this field, the association of osteo-inductive factors with implantable materials; as well as the association of osteogenic stem cells with these materials in the field of orthopaedic surgery are now booming. This paper aims to review the progression in biomaterials and the several therapeutic strategies in order to examine biomaterial interactions at the cellular and wider host level. Moreover, the favorable properties of nanotechnology exploited in biomedical applications were widely focused on. In our opinion, these advances represent some of the few examples in which the progress of molecular biology has a good chance of early clinical success.

1. Introduction

With the increase in the percentage of aging population worldwide, the number of individuals suffering from physical disability is also on the rise. This increase drives the demand for biomaterials products and open more doors to the development of a new tissular engineering strategy. In fact, the global market for materials products was valued at $13.8 billion in 2011 and is projected to reach nearly $14.7 billion, and $19.5 billion in 2017, a five-year compound annual growth rate (CAGR) of 5.9%. The industrial sector as well as other ones are projected to total nearly $5.6 billion in 2012 and $7.9 billion in 2017, a CAGR of 7.1% (Fa-Ming et al. 2010). In the early part of the twentieth century, naturally derived materials began to be replaced by synthetic polymers, ceramics and metal alloys, which provided better performance, increased functionality and more reproducibility than their naturally derived counterparts (Jeong et al. 2013 , Jeong et al. 2009 , Lin et al. 2008). The development of biomaterials for tissue engineering applications has recently focused on the design of biomimetic materials that are able to interact with surrounding tissues by biomolecular recognition (Chan et al. 2008). In this regard, as cell and molecular biology converge with materials science and biomedical engineering, new applications in regenerative medicine benefited from interactive biomaterials serving to orchestrate cell attachment and growth. For example, biomaterials can be implanted with a combination of specific cell types as a cell delivery vehicle, be utilized as a drug carrier to activate a specific cellular function in the localized region (Chan et al.2008, Catledge et al.2004, Heuts et al.2010, Tang et al.2013, Weis et al.2013, Seeto et al.2013). On the other hand, nanotechnology, which first appeared in the twentieth century, is an area of science devoted to the manipulation of materials atoms and molecules of materials in the nanometer range. Therapeutic uses of nanoparticles are among the most recent developments including all particles that possess at least one dimension that is less than 100 nm. It has been shown that the remarkable recognition capabilities of biomolecules when combined with the unique properties of nanomaterials can lead to novel tissue substitutes, biological electronics such as biosensors, sensitive diagnostic systems, and controlled drug delivery systems with significantly improved performances. This paper comprehensively covers literature reports which have investigated specifically the current state of the art, starting with current products of usual graft substitutes and moving onto recent developments and novel therapeutic approaches in clinical setting of tissue engineering as shown in Figure 1.

2. Advances in biomaterials

2.1. First generation

Traditional biomaterials employed in bone defect management consist in the use of autografts, allografts or xenografts [Kivovics et al.2013, Marquardt et al.2013). Despite all the satisfactory results, these therapies present limitations such as material availability, donor site morbidity, anatomic problems and the risk of inducing transmissible diseases (Vining et al.2012). These complications prompted research activities to provide alternatives to conventional tissue grafting. A strong interest in use of ceramics for biomedical applications appeared in the late 1960's (Dorozhkin et al .2010). Used initially as alternatives to metals in order to increase a biocompatibility of implants, bioceramics have become a diverse class of biomaterials, presently including three basic types, relatively bioinert ceramics, bioactive and bioresorbable ones (Rey et al .2009). Among these biomaterials, biphasic calcium phosphate (BCP) ceramics are used successfully in human surgery because their chemical composition is closely related to that of bone mineral (Rey et al .1995). These ceramics are biocompatible, osteoconductive, and degradable through a chemical and cellular process. Macroporosity of calcium phosphate (CaP) blocks facilitates bone colonization in both the deep and peripheral parts of the implants. Improvements in CaP biotechnology and new therapeutic approaches such as percutaneous or minimal-invasive techniques in radiology, orthopedics (Hrubina et al.2013)and spinal surgery, allowed the development of injectable CaP biomaterials for bone replacement. This launched the field of bioactive ceramics, with many new materials and products being formed from variations on bioactive glasses and also glass–ceramics.The first bioactive glass was invented by Larry Hench at the University of Florida in 1969 (Larry et al.2006). The mechanism of bonding of bioactive glasses (composed of Na_2O–aO–P_2O_5–SiO_2) to living tissue, established in 1971 (Hench et al.1997). The main discovery was that of a glass having the composition 46.1 mol. % SiO_2, 24.4 mol.% Na_2O, 26.9 mol.% CaO and 2.6 mol.% P_2O_5, later termed 45S5 (Hench et al.1997). These bioactive glasses, exhibit unique properties for this application showing ability to bond to soft tissue as well as to hard tissue and to form a carbonated hydroxyapatite layer (HCA) when

exposed to biological fluids (Jebahi et al.2012, Dietrich et al. 2012, Oudadesse et al. 2011). More recently, a second generation of biomaterials has been developed. Bioactive materials elicit a controlled action and therapeutic responses in the physiological environment are widely studied in the remainder of this work.

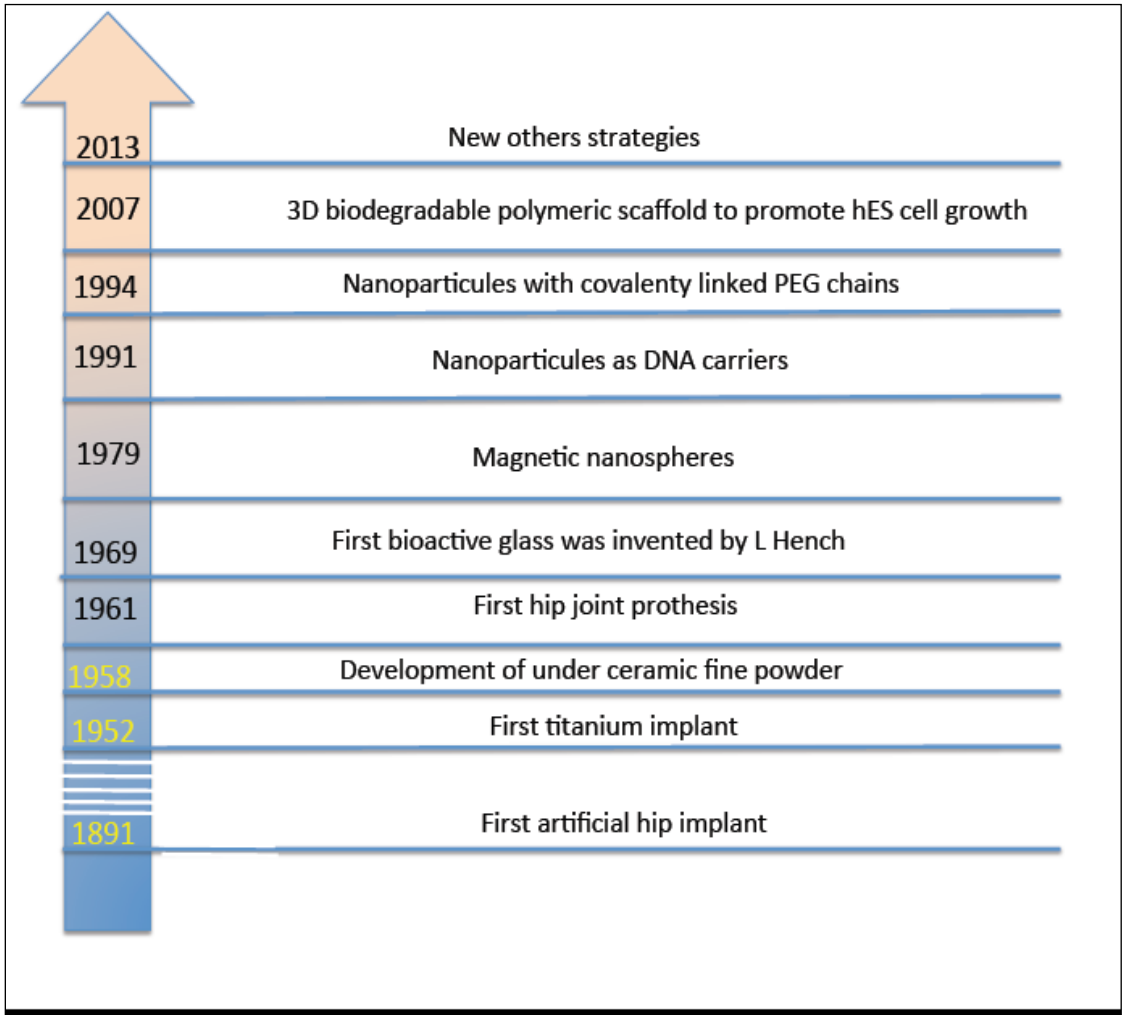

Fig. 1. development of biomaterials for tissue engeneering .

2.2. Second generation

Great progress in structure control and functionalization design has been achieved for biomedical applications. Recently, much attention has been paid to the molecules delivering properties in tissue engineering. As the science of biotechnology keeps advancing, researchers are exploring different materials for various biomedical applications and local gene delivery systems.

2.2.1. Ions release

Due to the benefic influence of some ion on the health tissue disease, some study was concentrated on the influence of some inorganic element. Phosphorous (P) (Gough et al. 2002), Silicon (Si) (Zhang et al. 2013, Fouad et al. 2013), Strontium (Sr) [Jebahi et al. 2013, Jebahi et al. 2012), Zinc (Zn) (Cheng et al. 2013, Geilich et al. 2013) as well as Boron (B) (Wang et al. 2008, Uysal et al. 2009), Vanadium (V) (Kim et al. 2012) , Cobalt (Co) [Lee et al. 2013, Ignjatović et al. 2013] and Magnesium (Mg) (Yang et al. 2008) are known to be involved in the bone metabolism and to play a physiological role in angiogenesis, growth and mineralization of bone tissue. In particular, metal ions act as enzyme co-factors and therefore influence signalling pathways and stimulate metabolic effects occurring

during tissue formation (Naik et al. 2013, Sobczak-Kupiec et al. 2012). These effects make metal ions attractive for use as therapeutic agents in the fields of hard and soft tissue engineering (Caridade et al. 2013). Moreover, Ca and P, bone apatite is substituted by many different trace elements occurring in smaller concentration. Hence, several ions have been considered to be promising agents in enhancing the bone-forming ability of implant materials and scaffolds, which can be achieved by controlling the release of specific ions during in vivo dissolution of the scaffold. In previous studies, a new developed type of Sr-incorporated hydroxyapatite, glass cement (Sr-HAC, 46S6Sr) have been studied (Okayama et al.1991, Oudadesse et al.2011). The Sr-HAC's in vivo biocompatibility, including acute toxicity, hemolytic reaction, pyrogen reaction, and cytoxicity has been evaluated, during intramuscular and femoral implantation. In this study, the optical transmission photographs show that the Sr doses play an important role on the interface between the implants and the new bone. The energy dispersion X-ray spectrum analysis indicates that there exists a gradient distribution of Sr element in the tight and bioactive interface between the implants and the new bone. This result indicates that the Sr element takes a share in the mineralization of the new bone together with Ca element. The bioactive glass is found as a therapeutic biomaterial protecting against oxidative stress for application in tissue engineering. Zinc is also known to play an important role in bone metabolism (Hackenberg et al.2013) and to have anti-inflammatory effects. Furthermore, Zinc-containing bioactive glasses stimulates bone formation in vitro by activating protein synthesis in osteoblast cells and increasing ATPase activity in bone (Yan et al.2013). Moreover, Zn shows inhibitory effect on bone resorption inhibiting the formation of osteoclast cells in mouse marrow cultures. The regulatory effects of Zn on bone cells has suggested also the importance of role in gene expression. Copper (Cu) has been shown to play a significant role in angiogenesis . For example, remarkable distributions of cellular Cu have been found in human endothelial cells when they were induced to undergo angiogenesis revealing the importance of the ion as angiogenic agent (Maeyama et al.2005 , Naghiu et al.2013).

2.2.2. Antibacterial carriers

It is acknowledged that medical device related infections account for a substantial morbidity as well as causing a sharp increase in health-care costs. Biofilms cause pipe plugging and corrosion and are responsible for causing important economic losses by damaging equipment and contamination of biomaterials. Removal of damaged material is a solution in both industrial and medical fields. Achievement of infection-resistant materials can be based on different strategies, (i) modification of the biomaterial surface to give anti-adhesive properties, (ii) doping the material with antimicrobial substances, and (iii) combining anti-adhesive and antimicrobial effects in the same coating. Furthermore, another requirement to be reached is (iv) the realization of a material able to oppose biofilm formation and, at the same time, to support bone repair. One of the strategies to prevent the bacterial attachment and biofilm formation is to kill the bacterial cells when they come in contact with the polymeric surfaces . Treatment of these infections often requires multiple operations, device removal, long-term systemic antibiotics, and extended rehabilitation, and is frequently ineffective, leading to worse clinical outcomes and increased financial costs (Chang et al.1992). Hence previous studies mixed bactericidal and fungicidal agents with polymethyl methacrylate (PMMA), and other polymers to reduce the bacterial infections (Chang et al.1992). Other strategies include the use of molecules which can dissolve biofilms (Kulkov et al.2013), or change the surface energy of the polymer. The second strategy is mainly based on the local delivery of antibiotics through carrier biomaterials and the risk of eliciting antibiotic resistance have been extensively discussed in Campoccia et al (Liu, et al.2012). Besides antibiotics, chitosan also has been proven to be effective as an antimicrobial coating. Morever, different sophisticated technologies have been studied for its grafting on material)surface (Sivakumar et al.2010, Hansson et al.2012, Gao et al.2012, Sivakumar et al.2012. Nanoparticles are defined as clusters of atoms whose size ranges from 1 to 100 nm, characterized by a very large surface area to volume ratio. Copper, zinc, magnesium and especially silver and gold nanoparticles display an antibacterial activity (Shameli et al. 2012, Erriu et al. 2013, Lin et al. 2006, Varkey et al. 2004). The antimicrobial activity of titanium oxide (TiO2) and of silver oxide (Ag2O) nanoparticles can be enhanced by irradiation with visible light (Tayalia et al. 2009). A comprehensive review on the photoinduced catalytic mechanisms of TiO2 and on its antibacterial activity, also against biofilm-embedded bacteria, has been recently presented (Langer et al. 1998). The use of TiO2 as a photocatalyst is limited to medical devices reachable by visible light irradiation (>400 nm).

3. Nanobiomaterial

The nanomaterials level is the most advanced at present, both in scientific knowledge and in commercial applications (Berger et al. 2011; Panyala et al. 2009; Panyala et al. 2008). A decade ago, nanoparticles were studied because of their size-dependent physical and chemical properties . Now they have entered a commercial exploration period . Nanomaterials have unique surface properties and energetics due to higher surface areas, higher surface roughness, higher amounts of surface defects (including grain boundaries), altered electron distributions, etc. All of these unusual properties inherent for nanomaterials will affect interactions with proteins since all proteins are nanoscale entities. Recently, Cheng et al. reported that human cartilage cells attached and proliferated well on HA nanocrystals homogeneously dispersed in polylactic acid (PLA) composites (Nandi et al.2008). Matthews et al. demonstrated that type II of collagen could be electrospun to form nonwoven fibrous scaffolds with fiber diameters ranging from 110 nm to 1.8 μm to support chondrocyte growth and infiltration (Santos et al.2007) . Even anodized metals (such as Ti) possessing nanometer pores increase chondrocyte adhesion and migration (Chen et al.2012) . In a very enhanced strategy of biomaterial use, nanoparticles are being designed to exploit the chemical and physical differences between normal and tumour-associated vasculature in order to concentrate the particles selectively within or near tumours, allowing subsequent drug-induced cell death. Recent demonstrations of polymeric nano particles could be designed for trafficking through the lymphatic vessels to target T cells in the lymph nodes. The synergistic enhanced effect of the relevant gold nanoparticles on the drug uptake of target cancer cells could provide a new strategy to inhibit the multidrug resistance of the respective cancers (Zeng et al.2013, Rajeswari et al.2009). Magnetic nanoparticles were also used for improving cell invasion in tissue engineering. Ion flows caused by electromechanical stimulation could probably modulate regeneration, suggesting that electrochemical signals could be used to alter cell fate directly and by manipulating biomaterial structure and presentation of chemical epitopes indirectly (Kadriye et al.2009). In another study, PMMA-based cements containing magnetite (C-PMMA/Fe3O4) was found to be useful in hyperthermia treatment for bone tumor. These investigations are useful for designing new PMMA/Fe3O4 bone cement with high heating efficiencies and biocompatibilities for bone tumor treatments. C-PMMA/Fe3O4 was prepared by incorporating Fe3O4 powders of different diameters (means of 300, 35, and 11 nm) into the polymerization reaction of PMMA to develop new bone cement with high heating efficiencies in alternating current magnetic fields (Fabio et al. 2011, Chao et al. 2012).

4. Conclusion

The highly widespread illnesses and accidents offered much inspiration for the novel biomaterial design that can stimulate cellular regeneration and functional recovery. Many experts agree that the greatest hope for treatment of the damaged tissues will involve a combinatorial approach that integrates biomaterial scaffolds, cell transplantation, and molecule delivery. This contuning research progresses permits the discovery of new biomaterials that may provide yet another opportunity to address clinical needs. Moreover, the nanotechnology has distinct properties that make the nanostructures potential candidates for different nanoscale bio-medical and sensor device applications. This devellepement in biomaterial design is encouraging, but new materials that provide tunable platforms addressing multiple key scaffold design criteria are currently needed. Progress toward the design and optimization of such scaffolds may potentially be hastened through more collaboration, better in vitro three-dimensional models, and more standardized in vivo animal models.

References

Berger, J.C., 2011. The age of biomedicine, current trends in traditional subjects J Appl. Biomed., 9 , p 57-61.

Bui, X.V., Oudadesse, H., Le Gal, Y., 2012. Merdrignac-Conanec, Cathelineau O. G., Sol-gel synthesis of a new composition of bioactive glass in the quaternarysystem SiO2-CaO-Na2O-P2O5Korean. J. Chem. Eng., 29, 215-220.

Chen, A.Z., Chen, M.Y., Wang, S.B., Huang, X.N., Liu, Y.G., Chen, Z.X., 2012. Functional enhancement of chitosan and nanoparticles in cell culture, tissue engineering, and pharmaceutical applications. J. Appl. Polym. Sci., 124, 3728–3736.

Chang, Ch-C., Merritt, K., 1992. Microbial adherence on poly (methyl methacrylate) (PMMA) surfaces . J. Biom. Mate. Res., A., 2, 197–207.

Chan, B.P., Leong, K.W.J., 2008. Scaffolding in tissue engineering, general approaches and tissue-specific considerations. Eur. Spine J. December., 17(Suppl 4), 467–479.

Catledge, S.A., Vohra, Y.K., Bellis, S.L., Sawyer, A.A., Nanosci, J., 2004. Nanotechnol., 4,986–9.

Cheng, J., Liu, B., Wu, Y.H., Zheng, Y.F., 2013. omparative in vitro Study on Pure Metals (Fe, Mn, Mg, Zn and W) as Biodegradable Metals. J. Metals. Mater. Sci. Technol., 29, 619–627.

Caridade, S.G., Merino, E.G., Alves, N., Zea Bermudez, M., Boccaccini, V., Mano, A.R., 2013. Chitosan membranes containing micro or nano-size bioactive glass particles, evolution of biomineralization followed by in-situ dynamic mechanical analysis, J. Mech. Behav. Biomed. Mater., in press.

Chao, X., Zhang, Z., Guo, L., Zhu, J., Peng, M., Vermorken, A.J., Van de Ven, W.J., Chen, C., Cui, Y. A., 2012. Novel Magnetic Nanoparticle Drug Carrier for Enhanced Cancer Chemotherapy PLoS One 7() e40388.

Dorozhkin, S.V., 2010. Bioceramics of calcium orthophosphates. Biomaterials., 31, 1465-85.

Dietrich, E., Oudadesse, H., Lucas-Girot, A., Mami, M., 2009. In vitro bioactivity of meltderived glass 46S6 doped with magnesium. J. Biomed. Mater Res., A 88,1087, 96.

Danišovič, Ľ., Lesný, P., Havlas, V., Teyssler, P., Syrová, Z., Kopáni, M., Fujeríková, G., Tomáš, T., 2007. Eva Syková1,2, Pavla Jendelová1,2Chondrogenic differentiation of human bone marrow and adipose tissue-derived mesenchymal stem cells. J. Appl. Biomed., 5, p 139-150.

Erriu, M., Pili, F.M., Tuveri, E., Pigliacampo, D., Scano, A., Montaldo, C., Piras, V., Denotti, G., Pilloni, A., Garau, V., Orrù, G., 2013. il Essential Mouthwashes Antibacterial Activity against Aggregatibacter actinomycetemcomitans, A Comparison between Antibiofilm and Antiplanktonic Effects. Int. J. Dent., 13,164267.

Eckl, M.P., Bresgen, N., 2003. The cultured primary hepatocyte and its application in toxicol., 1, 117-126.

Fa-Ming, C.h., Jing, Z. , Min, Z.Y., Fang, C.h., Zhi-Fen, W., 2010, A review on endogenous regenerative technology in periodontal regenerative medicine Biomaterials, 31() 7892–7927.

Ferreira, M.S., Jahnen-Dechent, W., Labude, N., Bovi, M., Hieronymus, T., Zenke, M., Schneider, R.K., Neurs, S., 2012.Cord blood-hematopoietic stem cell expansion in 3D fibrin scaffoldswith stromal support Biomaterials., 33, 6987-97.

Fouad, H., Elleithy, R., Othman, Y., 2013. Alothman, Thermo-mechanical, Wear and Fracture Behavior of High-density Polyethylene/Hydroxyapatite Nano Composite for Biomedical Applications, Effect of Accelerated Ageing J. Mater. Sci. Technol., 29, 573-581.

Fikackova, H., Navratilova, B., Dylevsky, I., Navratil, L., Jirman, R., 2003. Assessment of the effect of non invasive laser on the process of healing of an extraction wound by infrared thermography, preliminary study., 1, p 175-180.

Fa-Ming, C., Min, Z., Zhi-Fen, W., 2010. Toward delivery of multiple growth factors in tissue engineering Biomater., 31, 6279-6308.

Fabio, V., John, B., Giovanna, O., Paulo, T.O., 2011. Rima Wazen, Antonio Nanci , Nanoscale surface modifications of medically-relevant metals, state-of-the art and perspectives Nanoscale., 3, 335–353.

Gough, J.E., Christian, P., Scotchford, C.A., Rudd, C.D., Jones, I.A., 2002. Synthesis, degradation, and in vitro cell responses of sodium phosphate glasses for craniofacial bone repair. J. Biomed. Mater. Res., 59 ,481e9.

Geilich, B.M., Webster, T.J., 2013. Reduced adhesion of Staphylococcus aureus to ZnO/PVC nanocomposites. Int. J. Nanomed., 8, 1177-84.

Gao, W., Lai, J.C., Leung, S.W., 2012. Functional enhancement of chitosan and nanoparticles in cell culture, tissue engineering, and pharmaceutical applications Front Physiol., 3, 321.

Hackenberg, S., Scherzed, A.A., 2013. Functional responses of human adipose tissue-derived mesenchymal stem cells to metal oxide nanoparticles in vitro. Technau, K., Froelich, R., Hagen, N., Kleinsasser. J. Biomed. Nanotechnol., 9, 86-95.

Hrubina, M., Horak, Z., Bartoska, R., Navratil, L., Rosina, J., 2013. Computational modeling in the prediction of Dynamic Hip Screw failure in proximal femoral fractures. J. Appl. Biomed., 11, p 143-151.

Hench, L.L., 2006. The story of Bioglass_R. J. Mater. Sci. Mater. Med., 17,967–978.

Hench, L.L., Clark, A.E., JR, H.F., 1997. Schaake, Effects of microstructure on the radiation stability of amorphous semiconductors. Int. J. Non-Cryst. Sol., 28,10 837.

Hu, X., Park, S.H., Gil, E.S., Xia, X.X., Weiss, A.S., Kaplan, D.L., 2011. The influence of elasticity and surface roughness on myogenic and osteogenic-differentiation of cells on silk-elastin biomaterials. Biomaterials., 32,8979-89.

Huebsch, N., Mooney, D.J., 2009. Inspiration and application in the evolution of biomaterials. Nature., 26, 426-32.

Heuts, J., Salber, J., Goldyn, A.M., Janser, R., Moller, M., Klee, D., 2010. Biomed. Mater. Res., A. 92() 1538-51

Hansson, A., Francesco, T.D., Falson, F., Rousselle, P., Jordan, O., Borchard, G., 2012. Preparation and evaluation of nanoparticles for directed tissue engineering. Int. J. Pharm., 15, 73-80.

Ignjatović, N., Ajduković, Z., Savić, V., Najman, S., Mihailović, D., Vasiljević, P., Stojanović, Z., Uskoković, V., Uskoković, D., 2013. Nanoparticles of cobalt-substituted hydroxyapatite in regeneration of mandibular osteoporotic bones. J. Mater. Sci. Mater. Med., 24, 343-54.

Heo, D.N., Yang, D.H., Moon, H.J., Lee, J.B., Bae, M.S., Lee, S.C,. Lee, W.J., Sun, I.C., Kwon, I.K., 2012.Gold nanoparticles surface-functionalized with paclitaxel drug and biotin receptor as theranostic agents for cancer therapy. Biomaterials., Jan. 33(3), 856-66.

Jeong, K., Park, S., Lee, Y.D., Lim, C.K., Kim, J., Chung, B.H., Kwon, I.C. Park, C.R., Kim, S., 2013. Conjugated Polymer/Photochromophore Binary Nanococktails, Bistable Photoswitching of Near-Infrared Fluorescence for In Vivo Imaging. Adv Mater. [Epub ahead of print].

Jebahi, S., Saoudi, M., Badraoui, R., Rebai, T., Oudadesse, H., Ellouz, Z., Keskese, H., El Feki, A., El Feki, H., 2012. Biologic Response to Carbonated Hydroxyapatite Associated with Orthopedic Device, Experimental Study in a Rabbit Model Korean. J. Pathol., 46, 48-54

Jebahi, S., Oudadesse, H., Bui, X.V., Keskes, H., Rebai, T., El Feki, A., Feki, H.E., 2012. Repair of bone defect using bioglass-chitosan as a pharmaceutical drug, An experimental study in an ovariectomised rat. model. Afr. J. Pharm. Pharmacol., 16,1276 – 1287

Li, X., Zhao, D., Zhang, F., 2013. Theranostic Upconversion Nanoparticles Theranostics., 3(5),292-305.

Jebahi, S., Oudadesse, H., Jardakd, I., Khayata, H., Keskes, A., Khabire, T., Rebaid, H., El Fekic, A., 2013. El Feki. Ann Pharm Fr, (2013), http,//dx.doi.org/10.1016/j.pharma. 05.003.

Jebahi, S., Oudadesse, H., El Feki, H., Rebai, T., Keskes, H., Pascal, P., et al., 2012. Antioxidative/oxidative effects of strontium-dopedbioactive glass as bone graft, in vivo assays in castrated rats. J. Appl. Biomed., 10,195—209.

Kim, Y.S., Song, M.Y,, Park, E.S., Chin, S., Bae, G.N., Jurng, J., 2012. Visible-light-induced bactericidal activity of vanadium-pentoxide (V2O5)-loaded TiO2 nanoparticles. Appl. Biochem. Biotechnol., 168, 1143-52

Kadriye, T., Rui, R.L., 2009. Biodegradable Polymeric Fiber Structures in Tissue Engineering Tissue eng part b rev 15, 17-27.

Kulkova, J., Abdulmajeed, A.A., Könönen, E., Närhi, T.O., 2013. The effect of exposed glass fibers and particles of bioactive glass on the surface wettability of composite implants J. Appl. Biomater. Funct. Mater., [Epub ahead of print].

Shameli, K., Bin Ahmad, M., Zargar, M., Yunus, W.M., Ibrahim, N.A., Shabanzadeh, P., Moghaddam, MG., 2011. Synthesis and characterization of silver/montmorillonite/chitosan bionanocomposites by chemical reduction method and their antibacterial activity. Int. J .Nanomed., 6, 271–284.

Kivovics, M., 2013. Osteobiol and other bone graft materials used in Hungary, Osteobiol" and other bone graft materials used in Hungary. Fogorv Sz., 106, 33-8

Lucas-Girot, A., Mezahi, F.Z., Mohamed, M., Oudadesse, H., Harabi, A., 2011. Le Floch Marie. J. N-Crys Sol., 357, 3322-3327.

Liu, Y., Zheng, Z., Zara, J.N., Hsu, C., Soofer, D.E., Lee, K.S., Siu, R.K., Miller, L.S., Zhang, X., Carpenter, D., Wang, C., Ting, K., Soo, C., 2012. The antimicrobial and osteoinductive properties of silver nanoparticle/poly (DL- lactic-co-glycolic acid)-coated stainless steel Biomaterials., 33, 8745-56.

Lin, G.Y., Zhang, Z.F., Zhang, H., Peng, D.S., Zhou, J., 2008. Study on the Hot Deformation Dehaviors of Al-Zn-Mg-Cu-Cr Aluminum Alloy G.Y. Lin; Z.F. Zhang; H. Zhang Acta metall sin-Engl., 21, 109-115.

Lin, S.S., Landesberg, R., Chin, H.S., Lin, J., Eisig, S.B., Lu, H.H., 2006. Controlled release of PRPderivedgrowth factors promotes osteogenic differentiation of human mesenchymal stem cells.Conf Proc IEEE. Eng. Med. Biol. Soc., 1,4358-61.

Li, Z., Kawamura, K., Kawashita, M., Kudo, T.A., Kanetaka, H., Hiraoka, M., 2012. In vitro assessment of poly(methylmethacrylate)-based bone cement containing magnetite nanoparticles for hyperthermia treatment of bone tumor. J. Biomed. Mater. Res. A., 100, 2537-45.

Lee, I.H., Yu, H.S., Lakhkar, N.J., Kim, H.W., Gong, M.S., Knowles, J.C., Wall, I.B., 2013. Development, characterisation and biocompatibility testing of Development, characterisation and biocompatibility testing of a cobalt-containing titanium phosphate-based glass for engineering of vascularized hard tissues. Mater. Sci. Eng. C. Mater. Biol. Appl., May 1, 33(4), 2104-12.

Langer. R., 1998. Drug delivery and targeting. Nature., 392,5e10.

Marquardt, L.M., Sakiyama-Elbert, S.E., 2013. Engineering peripheral nerve repair. Curr. Opin. Biotechnol., [Epub ahead of print].

Maeyama, R., Kwon, I.K., Mizunoe, Y., Anderson, J.M., Tanaka, M., Matsuda, T., 2005. Novel bactericidal surface, Catechin-loaded surface-erodible polymer prevents biofilm formation. J. Biomed. Mater. Res., A. 75, 146-55.

Naghiu, M.A., Gorea, M., Mutch, E., Kristaly, F., Tomoaia-Cotisel, M., 2013. Forsterite Nanopowder, Structural Characterization and Biocompatibility Evaluation J. Mater. Sci. Technol., 29, 628-632.

Nandi, S.K., Kundu, B., Ghosh, S.K., De, D.K., Basu, D., 2008. Efficacy of nano-hydroxyapatite prepared by an aqueous solution combustion technique in healing bone defects of goat. J. Vet .Sci., 9, 183-91.

Naik, K., Chatterje, A., Prakash, H., Kowshik, M., 2013. Mesoporous TiO2 nanoparticles containing Ag ion with excellent antimicrobial activity at remarkable low silver concentrations. J. Biomed Nanotechnol., 9, 664-73.

Oudadesse, H., Dietrich, E., LGal, Y., Pellen, P., Bureau, B., Mostafa, A.A., 2011. Cathelineau G.Apatite forming ability and cytocompatibility of pure and Zn-doped bioactive glasses Biomed Mater., 3,035006.

Okayama, S., Akao, M., Nakamura, S., Shin, Y., Higashikata, M., Aoki, H., 1991. The mechanical properties and solubility of strontium-substituted hydroxyapatite. Biomed. Mater. Eng., 1, 11-7.

Oudadesse, H., Dietrich, E., Bui, X.V., Le gal, Y., Pellen, P., Cathelineau, G., 2011. Investigation of the surface reactivity of a sol–gel derived glass in the ternary system SiO2–CaO–P2O5 App. Surf. Sci., 1, 8587-8593.

Panyala, N.R., Pena-Mendez, E.M., 2009. Havel J Gold and nano-gold in medicine, overview, toxicology and perspectives. J. Appl. Biomed., 7, p 75-91

Panyala, N., Pena-Mendze, E., Havel, J., 2008. Silver or silver nanoparticles, a hazardous threat to the environment and human health? 6, p 117-129 J Appl Biomed.

Rey, C., Combes, C., Drouet, C., Glimcher, M.J., 2009. Bone mineral, update on chemical composition and structure. Osteoporos Int., 20, 1013–1021.

Rey, C., Miquel, J., Facchini, L., Legrand, A., et al., 1995. Hydroxyl groups in bone mineral. Bone., 16,583–586.

Rajeswari, R., Susan, L., Clarisse, C.N., Casey, K.C., Michael, R.R., 2009. Seeram Effects of nanotopography on stem cell phenotypes World J. Stem. Cells., 31, 55–66.

Seeto, W.J., Tian, Y., Lipke, E.A., 2013. Peptide-grafted poly(ethylene glycol) hydrogels support dynamic adhesion of endothelial progenitor cells. Acta Biomater. [Epub ahead of print].

Sobczak-Kupiec, A., Malina, D., Piatkowski, M., Krupa-Zuczek, K., .Wzorek, Z., Tyliszczak, B., 2012. Physicochemical and biological properties of hydrogel/gelatin/hydroxyapatite PAA/G/HAp/AgNPs composites modified with silver nanoparticles. J. Nanosci. Nanotechnol., 12, 9302-11.

Sivakumar, P.M., Prabhawathi, V., Doble, M., 2010. QSAR SAR. Antibacterial activity and QSAR of chalcones against biofilm-producing bacteria isolated from marine waters. Env. Res., 21,247-63.

Sivakumar, P.M., Cometa, S., Alderighi, M., Prabhawathi, V., Doble, M., Chiellini, F., 2012. Carbohydrate Polymers. Chalcone embedded polyurethanes as a biomaterial, Synthesis, characterization and antibacterial adhesion 1 4 () 353-360.

Santos, M.H., Valerio, P., Goes, A.M., Leite, M.F., Heneine, L.G., Mansur, H.S., 2007.Biocompatibility evaluation of hydroxyapatite/collagen nanocomposites doped with Zn+2Biomed Mater 2() 135-41.

Shan, Y., Luo, T., Peng, C., Sheng, R., Cao, A., Cao, X., Shen, M., Guo, R., Tomas, H., Shi, X., 2012. Gene delivery using dendrimer-entrapped gold nanoparticles as nonviral vectors. Biomater. Biomater., 33, 3025-35.

Tang, Z., Xie, Y., Yang, F., Huang, Y., Wang, C., Dai, K., Zheng, X., Zhang, X., 2013. Porous Tantalum Coatings Prepared by Vacuum Plasma Spraying Enhance BMSCs Osteogenic Differentiation and Bone Regeneration In Vitro and In Vivo. PLoS One., 8, e66263.

Tayalia, P., Mooney, D.J., 2009. Controlled architectural and chemotactic studies of 3D cell migration Adv Mater 21, 3269e85.

Ramos, J.F., Webster, T.J., 2012. Int. J. Nanomedicine. Cytotoxicity of selenium nanoparticles in rat dermal fibroblasts 7,3907-14.

Thein-Han, W.W., Saikhun, J., Pholpramoo, C., Misra, R.D., Kitiyanant, Y., 2009. Chitosan-gelatinscaffolds for tissue engineering, physico-chemical properties and biological response of buffalo embryonic stem cells and transfectant of GFP-buffalo embryonic stem cells Acta Biomater., 5, 3453-66

Teng, Y., Hu, Y., Li, X., Guan, Y., Gui, J., 2011. Ectopic osteogenesis with immortalized human bone marrow stromal stem cells and heterologous bone. J. Appl. Biomed., 9, 111-118.

Unger, R.E., Sartoris, A., Peters, K., Motta, A., Migliaresi, C., Kunkel, M., Bulnheim, U., Rychly, J.C.J., 2007. Tissue-like self-assembly in cocultures of endothelial cells and osteoblasts and the formation of microcapillary-like structures on three-dimensional porous biomaterials Biomaterials., 28, 3965–3976.

Uysal, T., Ustdal, A., Sonmez, M.F., Ozturk, F., 2009. Stimulation of bone formation by dietary boron in an orthopedically expanded suture in rabbits. Orthod., 79, 984e90.

Wang, S.L., Hong, L.L., Yu, W.W., 2008. Influence of 2-butyne-1, 4-diol on the Structure andPerformance of the Co-Ni Alloy Plated by Electro-depositionActa metall sin-Engl., 21, 50-56.

Varkey, M., Gittens, S.A., Uludag, H., 2004. Growth factor delivery , anupdate. Expert. Opin. Drug. Deliv., 1,19e36.

Vining, N.C., Warme, W.J., Mosca, V.S., 2012. Comparison of structural bone autografts and allografts in pediatric foot surgery J Pediatr Orthop., 32, 719-23.

Weis, S., Lee, T.T., Del Campo, A., García, A.J., 2013. Dynamic cell-adhesive microenvironments and their effect on myogenic differentiation. Acta Biomater., [Epub ahead of print].

Yang, Z., Li, J.P., Zhang, J.X., Lorimer, G.W., Robson, J., 2008. Review on Research and Development of Magnesium AlloysActa metall sin-Engl., 21, 313-328.

Yan, L.S., Jiang, W., Duan, W.J., Zheng, D., Wu, Z.L., Guo, W.F., Wang, Y.S., 2013. Morphology variation and optical properties of ZnO nanostructures grown using bio-template. J. Nanosci. Nanotechnol., Feb., 13(2), 1304-8.

Yan, G., Wang, Y., He, X., Wang, K., Su, J., Chen, Z., Qing, Z., 2012. A highly sensitive electrochemical assay for silver ion detection based on un-labeled C-rich ssDNA probe and controlled assembly of MWCNTs.Talanta., 94()178-83.

Zeng, X., Tao, W., Mei, L., Huang, L., Tan, C., Feng, S.S., 2013. Cholic acid-functionalized nanoparticles of star-shaped PLGA-vitamin E TPGS copolymer for docetaxel delivery to cervical cancer Biomaterials., 34, 6058-67.

Zhang, M., Xia, L., Gu, Z., Xing, G., 2013. Comparative bio-effects of SiO2/Gd2O3 nanoparticles depending on their core-shell structures. J. Nanosci. Nanotechnol., 13, 1270-3.

Yamane, S., Iwasaki, N., Majima, T., Funakoshi, T., Masuko, T., Harada, K., Minami, A., Monde, K., Nishimura, S., 2005. Feasibility of chitosan-based hyaluronic acid hybrid biomaterial for a novel scaffold in cartilage tissue engineering. Biomater., 26, 611-9.