Scientific Bulletin. Series F. Biotechnologies, Vol. XVII, 2013
ISSN 2285-1364, CD-ROM ISSN 2285-5521, ISSN Online 2285-1372, ISSN-L 2285-1364

BIODEGRADABLE MATERIALS AND ITS APPLICATIONS IN MEDICAL TOOLS DEVELOPMENT – A REVIEW

Elisabeta Elena TĂNASE[1], Maria RÂPĂ[2], Ovidiu POPA[1]

[1]University of Agronomic Sciences and Veterinary Medicine Bucharest, Faculty of Biotechnologies, Department of Industrial Biotechnology, 59 Mărăşti Blvd., District 1, 011464, Bucharest, Romania
[2]SC ICPE Bistrita S.A, 7 Parcului Street, Bistrita, Romania

Corresponding author email: elena.eli.tanase@gmail.com

Abstract

Biopolymers are the preferred materials for biological and life science applications because of their high adaptability and compatibility with biological molecules and cells. Polymer-based biomaterials are widely used for medical applications due to the multiple physical and chemical properties of these materials. Biopolymers can be easily fabricated in various complex shapes and structures and additionally surface properties can be easily tuned. The concept of biodegradable plastics is of considerable interest with respect to solid waste accumulation and environment sustainability issues. Greater efforts have been made in developing degradable biological materials without any environmental pollution to replace oil-based traditional plastics. Among numerous kinds of degradable polymers, polylactic acid sometimes called polylactide, an aliphatic polyester and biocompatible thermoplastic, is currently a most promising and popular material with the brightest development prospect and was considered as the 'green' eco friendly material. In this review different types of available biopolymers and their usage in medical tools development will be described.

Keywords: *biopolymers, biodegradable, polylactic acid.*

INTRODUCTION

Biomaterials are sometimes characterized as materials used to construct artificial organs, rehabilitation devices, or implants to replace natural body tissues (Bauer et al., 2013). More specific, biomaterials are materials that are used in close or direct contact with the body to augment or replace faulty materials. In general, they can be classified into living or once living materials, which fit into the division of, for example, tissue engineering, and materials that are of a synthetic origin. Such biomaterials can be defined as inorganic or organic materials that are biocompatible and can be implanted in the human body to replace or repair failing tissue. In recent years, progress in many different fields has paved the way to creating innovative biomaterials to improve existing treatments and develop new ones for a higher quality of life. Biomaterials play an important role in human health.

Biopolymers are the main type of biomaterials. According to their degradation properties, biopolymers can be further classified into biodegradable and non-biodegradable biopolymers. Many implants, such as bone substitution materials, some bone fixing materials, and dental materials, should possess long term stable performance in the body. In recent years, developments in tissue engineering, regenerative medicine and controlled drug delivery have promoted the need of new properties of biomaterials with features of biodegradation (Huayu et al., 2012). Biologically derived and synthetic biodegradable biopolymers have attracted considerable attention.

This paper reviews recent refereed published literature, particularly associated with the characteristics of biomaterials which are important to medicine.

MATERIALS AND METHODS

With an ageing population, war and sports related injuries there is an ever-expanding requirement for hard tissue replacement such as bone. Engineered artificial scaffold biomaterials with appropriate mechanical properties, surface chemistry and surface topography are in a great demand for enhancing cell attachment, cell growth and tissue formation at such defect sites. Most of these engineering techniques are aimed to mimick the natural organization of the bone tissues and thereby create a conductive environment for bone regeneration. As the interaction between the cells and tissues with biomaterials at the tissue–implant interface is a surface phenomenon, surface properties play a major role in determining both the biological response to implants and the material response to the physiological condition. Therefore surface engineering of biomaterials is aimed to modify the material and biological responses through changes in surface properties while still maintaining the bulk mechanical properties of the implant (Sameer and Narendra, 2009). Implants not only have to be biosafe and biostable in terms of cytotoxicity and degradation, they also have to match with the biological requirements of any structural biocompatibility. In other words, shape, inner structure and design of an implant need to be adapted to the characteristics of the tissue to be replaced (Bauer et al., 2013).

Low cost manufacturing of polymeric microdevices for transdermal and subcutaneous drug delivery is also slated to have a major impact on next generation devices for administration of biopharmaceuticals and other emerging new formulations. These devices range in complexity from simple microneedle arrays to more complicated systems incorporating micropumps, micro-reservoirs, on-board sensors, and electronic intelligence (Ochoa et al., 2012).

The different classes of materials used for the fabrication of bioimplants and bio-devices can be broadly classified as metallic materials, *polymers*, ceramics, *composites* and *natural materials*.

Polymers are long chain molecules consisting of large number of small repeating units known as monomers. They belong to the family of macromolecules and represent the largest class of biomaterials. Polymers can be derived either from natural sources or from synthetic organic sources (Figure 1.), (Bauer et al., 2013). Polymers can be easily manufactured to various complex shapes and structures and additionally surface properties can be easily tuned. Polymers are widely used in biomedical applications due to the range of physical and chemical properties possible with these materials (Mark, 1996).

A *composite* consists of two or more materials each with distinct physical or chemical properties. It is designed to have a combination of best characteristic of each component material. Biomedical composites are often designed to provide superior mechanical and biological compatibility.

They can be classified based on the matrix material or on the bioactivity of the composites. Some promising medical applications of biomedical composites include their use in total joint replacements, spine rods, discs, plates, dental posts, screws, ligaments and catheters (Makarov et al., 2013).

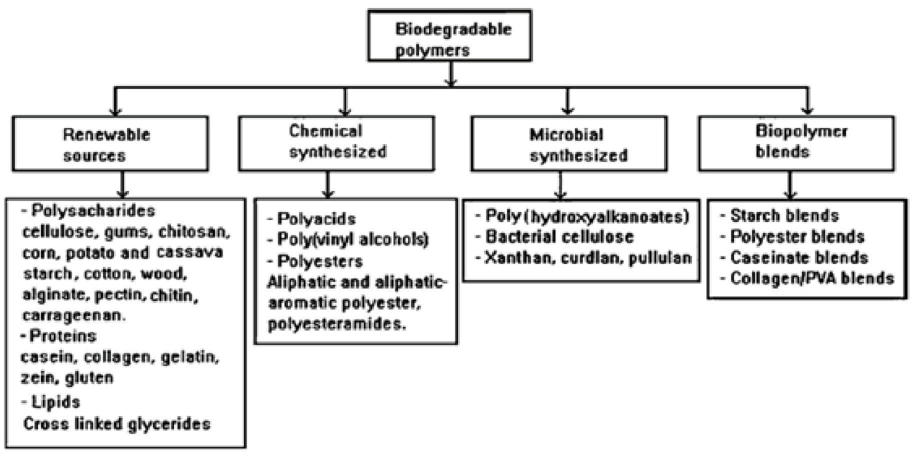

Figure 1. Clasification of biodegradable polymers and their nomenclature (Kestur et al., 2009)

Natural polymers such as starch, collagen, chitosan and glycosaminoglycans (chondroitin sulphate, hyaluronic acid) are the most commonly used natural materials for clinical applications (Liu et al., 1999).
Starch is a potentially useful polymer for the thermoplastic biodegradable materials because of its low cost, availability and production from renewable resources (Pal et al., 2006).
Collagen is a fibrous protein that connects and supports other bodily tissues such as skin, bone, tendons, muscles, and cartilage.
It is the wealthy available protein present in the bodies of mammals, including humans.
Chitosan is a natural biopolymer derived from crustacean and structurally similar to hyaluronic acid, a polymer component of the extracellular matrix (ECM), making it particularly attractive for tissue engineering (Foster and Butt, 2011; Mourya et al., 2011).
Glycosaminoglycan is the most abundant heteropolysaccharide present in the body. Condroitin Sulphate (CS) plays a key role in biomaterials field: it is a widely distributed glycosaminoglycan in the human body, structurally present in cartilage and other tissues such as eye, aorta, skeletal muscle, lung and brain. In biomedical applications, CS has shown *in vivo* anti-inflammatory effect. However the most commonly exploited natural polysaccharide in scaffold assembly for tissue engineering and as component for implant materials is hyaluronic acid (HA). HA, in fact, present a high capacity for lubrication, is very hydrophilic and influences several cellular functions such as migration, adhesion and proliferation (Agostino et al., 2012).
The advantages associated with these natural biomaterials can be listed as follows (Sameer and Narendra, 2009) : i) these materials being similar to the macromolecular substances, get easily recognized by the biological environment and therefore deal metabolically; ii) problems of toxicity, chronic inflammation, and lack of recognition by cells which occurs mostly with synthetic materials can be avoided;
iii) these materials are biodegradable, and therefore they can be used for applications where it is desired to deliver a specific function for a temporary period of time.
Poly (vinyl alcohol) (PVOH) is generally prepared by the saponification of poly (vinyl ester) s, such as poly (vinyl acetate) (PVAc).
PVOH has gained increasing attention in the biomedical field due to its bioinertness (Yong-Woo et al., 2000). PVOH hydrogels resemble organic tissue and have a high elastic modulus even though their water content is very high.
Poly (lactic acid) (PLA), is a biodegradable, biocompatible and compostable polyester derived from renewable resources such as corn, potato, cane molasses and beet sugar. It has a bright future as an environmentally friendly thermoplastic. With the help of this green polymer industries will be able to close the carbon cycle, and their dependence on non-renewable fossil resources will be reduced considerably. Aliphatic polyesters such as PLA, derived from lactic acid (LA), 2-hydroxy-propionic acid, produced from renewable resources, has promising applications in packaging, consumer goods, fibers and in biomedicine because of its excellent mechanical properties, transparency, compostability and bio-safety.

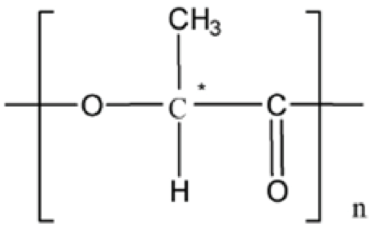

Figure 2. Structural formula of PLA, chiral molecule

Potential feedstock for the production of PLA is lactic acid (LA), which contains a chiral centre (Figure 2). LA can be produced by fermentation from renewable resources such as milk and carbohydrates such as corn, potato, cane molasses and beet sugar (Sameer and Narendra, 2009).

Poly (hydroxyalkanoate) (PHA). Another family of polyesters being studied widely are poly (hydroxyalkanoate) s (PHAs) that occur in nature. They are produced by a wide variety of micro-organisms as an internal carbon and energy storage, as part of their survival mechanism. Bacterially synthesized PHAs have attracted attention because they can be produced from a variety of renewable resources and they are truly biodegradable and highly biocompatible thermoplastic materials (Long et al., 2006).

RESULTS AND DISCUSSIONS

Biopolymers with reactive groups

-*Aliphatic polyesters*, such as poly (lactic acid) (PLA), poly (glycolic acid), poly (-ε capro-lactone) (PCL) and their copolymers, have been widely investigated for biomedical application because of their biodegradability, bioresor-bability and biocompatibility. They are among the most commonly used degradable materials for the preparation of clinical devices. Aliphatic polyesters with reactive groups have attracted attention because of the demand of synthetic biopolymers with tunable properties, including features such as hydrophilicity, biodegradation rates, bioadhesion, drug/targeting moiety attachment, etc. (Lou et al., 2003).

In particular, polymeric biomaterials with properties that can be tailored by introducing functional groups, such as carboxyl, hydroxyl, amino, ketal, bromo, chloro, carbon–carbon double bonds or triple bonds, etc., are needed.

-*Polycarbonate (PCs).* Since the last decade, polycarbonates (PCs) have attracted increasing attention in pace with their significant applications in the medical field, owing to their unique combination of biodegradability and biocompatibility. Polycarbonates have been commonly used as integral components of engineered tissues, medical devices and drug delivery systems (Feng et al., 2012).

-*Polyurethans* (PUs) are a large family of polymeric materials with an enormous diversity of chemical compositions, mechanical proper-ties, tissue-specific biocompatibility and biodegradability, with mechanical flexibility and moderate blood compatibility being their most prominent features. Because of their diversity of composition and mechanical properties, PUs are among the most extensively used synthetic polymers in biomedical applications, and remain one of the most popular groups of biomaterials applied to medical devices after half a century of use in the healthcare system (Chen et al., 2013).

-*Poly (amino acids)* is an important kind of biocompatible and biodegradable synthetic polymers and have been studied for biomedical application in many fields (Deming, 2007). However, their application is limited because of their insolubility or pH-dependent solubility and lack of functional groups.

-*Polyphosphoesters*. PPEs with repeating phosphoester units in the backbone are attractive biocompatibile and biodegradable biomaterials because of their structural similarity to the naturally occurring nucleic acid and easy functionality as compared to conventional polyesters (Zhao et al., 2003).

Biopolymers with responsive activities

-Due to the ability to mimick the basic response process of living systems, *stimuli-responsive polymers* have attracted increased attention. These polymers can respond to small changes (temperature, pH, photo, redox) in environ-mental stimuli with distinct transitions in phy-sical-chemical properties, including confor-mation, polarity, phase structure and chemical composition (Alarcon et al., 2005).

-*Electroactive biomaterials*. After the discovery that electrical signals can regulate cell attach-ment, proliferation and differentiation, many researchers sought to incorporate conducting polymers into biomaterials to take advantage of electrical stimuli.

- *Specific bonding biopolymers*. Alternative biodegradable platforms have been described in studies of nanoconjugate drug delivery poly-mers such as poly (l-glutamic acid) s, PLHis, polysaccharides, and PLLA, PLGA.

-*Biopolymers for tracing and bioimaging* (Bio-polymers for optical tracing and bioimaging, Biopolymers for MRI).

Specific biomedical applications

-*Medical devices*. Synthetic biodegradable polymers have attracted considerable attention for applications in medical devices, and will play an important role in the design and function of medical devices. The general criteria of polymer materials used for medical devices include mechanical properties and a degradation time appropriate to the medical purpose. In addition, the materials should not evoke toxic or immune responses, and they should be metabolized in the body after fulfilling their tasks. According to these requirements, various synthesized biodegradable polymers have been designed and used. Some synthesized biodegradable polymers that have been used or show potential in selected fields are summarized below.

▪ Drug-eluting stents (DES). DESs have been widely used as a default treatment for patients with coronary artery disease. Biodegradable polymers are always used as a biodegradable and bioresorbable coatings on stents to control the release of drugs. Besides being used as biodegradable coatings, biodegradable polymers are also candidate materials for fully biodegradable stents because of their suitable properties for controlled drug release and good mechanical performance to prevent stents from deforming or fracturing (Shen et al., 2012).

▪ Orthopedic devices. Orthopedic devices made from biodegradable materials have advantages over metal or nondegradable materials. They can transfer stress over time to the damaged area as it heals, allowing of the tissues, and there is no need of a second surgery to remove the implanted devices. Many commercial orthopedic fixation devices such as pins and rods for bone fracture fixation, and screws and plates for maxillofacial repair are made of PLLA, poly (glycolide) and other biodegradable polymers (Maharana et al., 2009; Mark, 1996).

▪ Disposable medical devices. In the 21st century, environment factors concern all manufacturing industries. Many disposable medical devices, such as syringes, injection pipes, surgical gloves, pads, etc., are usually made of non-degradable plastics, resulting in serious environmental and economic issues. PLA, poly (glycolide), poly [D,L- (lactide-co-glycolide)] and PCL are all biodegradable. Therefore, they are promising materials for use in disposable medical devices meeting environmental friendly requirements. These biodegradable polymers have been used to prepare some disposable medical devices and will likely have a widening commercial application.

▪ Other medical devices. Biodegradable polymers have also been used to prepare anastomosis rings used for intestinal resection, drug delivery devices, in situ forming implants and stents used in urology (Huayu et al., 2012; Mendez-Probst et al., 2010).

-*Tissue engineering*. Tissue engineering is an interdisciplinary field that applies the principles of engineering and life sciences towards the development of biological substitutes used to restore, maintain or improve tissue functions. The main purpose of tissue engineering is to overcome the lack of tissue donors and the immune repulsion between receptors and donors (Schmedlen et al., 2002; Kim et al., 2011).

- *Drug delivery and control release*. Biodegradable polymers, such as poly (α-malic acid), with reactive pendant carboxyl groups, can conjugate drugs (via ester or amide bonds) to form a biodegradable macromolecular prodrug to reduce the side-effects of free drugs. Drugs can be released via the degradation of biodegradable polymers (Crispim et al., 2012).

-*Gene delivery*. Gene delivery has great potential for treating various human diseases (Merdan et al., 2002). Recently, nonviral vectors have been proposed as safer alternatives to viral vectors for gene delivery. Many carriers are non-degradable and the risk arises of accumulation in the body, especially after repeated administration. A good gene carrier should be able to deliver the target gene to specific cells with high efficacy; it should also be degradable and be excreted from the body after a given time period. Recently, some research has evaluated non-degradable polymers with biodegradable polycations via hydrolysable linkers as gene carriers.

-*Bioseparation and diagnostics applications*. The development of biomedical polymers conjugated with peptide or protein domains has mostly focused on their use as bioactive materials in controlled drug delivery or tissue engineering. A new challenge arises in the development of materials for bioseparation and diagnostics applications. For these applications, materials that are biocompatible with reduced non-specific absorption and denaturation, that are able to amplify and transmit signals and that are beneficial for high-throughput screening with enhanced sensitivity and reduced size are in great demand. To meet these demands, polymeric materials in various shapes, such as membranes, thin films, micro/nano-particles, hydrogel and micro/nano-fibers have been widely investigated (Li et al., 2004).

CONCLUSIONS

Characterization of any material, particularly newly developed ones, is important from various standpoints, such as its utility and value addition, which may open up new areas for further development to assess the effectiveness of its processing, the effect of different environments on its properties and to find suitable areas of application.

Biodegradable biomaterials have been widely used and have greatly promoted the development of biomedical fields because of their biocompatibility and biodegradability.

Biodegradable polymers can be classified as natural or synthetic polymers according to the source.

Future integrated biorefineries based on green chemistry operations will serve as the basis for providing sustainable raw materials for biocomposite production.

The present and future look promising for the introduction of sustainable biocomposites as a replacement for traditional fossil based materials in diverse applications. A wide range of raw materials from recycled and renewable resources will be readily available for choice, together with controlled synthetic and modification routes to tailor the desired properties of the designed biocomposites (Vilaplana et al., 2010).

Once manufactured, products made from sustainable biocomposites must satisfy the requirement that no hazardous effects to the environment or to human health will be derived throughout their service life in the intended application. The development of biotechnology and medical technology has set higher requirements for biomedical materials. The development of commercially viable "green products" based on natural resources for both matrices and reinforcements for a wide range of applications is on the rise. This effort includes new pathways to produce natural polymers with better mechanical properties and thermal stability using nanotechnology and adding different natural fillers such as lignocellulosic fibers.

REFERENCES

Alarcon C.D.H., Pennadam S., Alexander C., 2005. Stimuli responsive polymers for biomedical applications. Chemical Society Reviews, 34, 276–285.

Agostino A.D., La Gatta A., Busico T., De Rosa M., Schiraldi C., 2012. Semi-interpenetrated Hydrogels Composed of PVA and Hyaluronan or Chondroitin Sulphate: Chemico-Physical and Biological Characterization. Journal of Biotechnology and Biomaterials, 2 (4).

Bauer S., Schmuki P., von der Mark K., Park J.,2013. Engineering biocompatible implant surfaces: Part I: Materials and surfaces. Progress in Materials Science, 58 (3), 261-326.

Chen Q., Liang S., Thouas G.A., 2013. Elastomeric biomaterials for tissue engineering. Progress in Polymer Science, 38 (3-4), 584-671.

Crispim E. G., Piai J. F., Fajardo A. R., Ramos E. R. F., Nakamura T. U., Nakamura C. V., Rubira A. F., Muniz E. C., 2012. Hydrogels based on chemically modified poly (vinyl alcohol) (PVA-GMA) and PVA-GMA/chondroitin sulfate: Preparation and characterization. eXPRESS Polymer Letters, 6 (5), 383–395.

Deming TJ., 2007. Synthetic polypeptides for biomedical applications. Progress in Polymer Science, 32, 858–875.

Feng J., Zhuo R.X., Zhang X.Z., 2012. Construction of functional aliphatic polycarbonates for biomedical applications. Progress in Polymer Science 37 (2), 211–236.

Foster L.J., Butt J., 2011. Chitosan films are NOT antimicrobial. Biotechnology Letters, 33, 417–421.

Huayu T., Zhaohui T., Xiuli Z., Xuesi C., Xiabin J., 2012. Biodegradable synthetic polymers: Preparation, functionalization and biomedical application. Progress in Polymer Science, 37 (2), 237-280.

Kestur G. S., Gregorio G.C. Arizaga, Wypych F., 2009. Biodegradable composites based on lignocellulosic fibers-An overview. Progress in Polymer Science, 34 (9), 982-1021.

Kim K.O., Akada Y., Kai W., Kim B.S., Kim I.S., 2011. Cells Attachment Property of PVA Hydrogel Nanofibers Incorporating Hyaluronic Acid for Tissue Engineering. Journal of Biomaterials and Nanobiotechnology, 2, 353-360.

Li H., Zhang Y., Chen X., Shi K., Yuan Z., Liu B., Shen B., He B., 2004. Synthesis and adsorption aspect of crosslinked PVA-based blood compatible adsorbents for LDL apheresis. Reactive and Functional Polymers, 58 (1), 53–63.

Liu L. S., Thompson A., Y., Heidaran M. A., Poser J. W., Spiro R. C., 1999. An osteoconductive

collagen/hyaluronate matrix for bone regeneration. Biomaterials, 20 (12), 1097–1108.
Long Y., Dean K., Lin L.,2006. Polymer blends and composites from renewable resources. Progress in Polymer Science, 31 (6), 576–602.
Lou X., Detrembleur C., Jérôme R., 2003. Novel aliphatic polyesters based on functional cyclic (di) esters. Macromolecular Rapid Communications, 24 (2), 161–172.
Maharana T., Mohanty B., Negi Y.S., 2009. Melt–solid polycondensation of lactic acid and its biodegradability. Progress in Polymer Science, 34 (1), 99-124.
Makarov C., Berdicevsky I., Raz-Pasteur A., Gotman I., 2013. In vitro antimicrobial activity of vancomycin-eluting bioresorbable b-TCP-polylactic acid nanocomposite material for load-bearing bone repair. Journal of Materials Science Materials in Medicine, 24 (3), 623-633.
Mark J. E., 1996. Physical properties of polymers handbook. Woodbury, NY: AIP Press.
Mendez-Probst C.E., Fernandez A., Denstedt J.D, 2010. Current Status of Ureteral Stent Technologies: Comfort and Antimicrobial Resistance. Current Urology Report, 11 (2), 67–73.
Merdan T., Kopeek J., Kissel T., 2002. Prospects for cationic polymers in gene and oligonucleotide therapy against cancer. Advanced Drug Delivery Reviews, 54, 715–758.
Mourya V.K., Inamdar N. N., Choudhari Y. M., 2011. Chitooligosaccharides: Synthesis, Characterization and Applications. Polymer Science, Ser. A, 53 (7), 583–612.
Ochoa M., Mousoulis C., Ziaie B., 2012. Polymeric microdevices for transdermal and subcutaneous drug delivery. Advanced Drug Delivery Reviews, 64 (14), 1603-1616.
Pal K., Banthia A.K., Majumdar D.K., 2006. Preparation of Transparent Starch Based Hydrogel Membrane with Potential Application as Wound Dressing. Trends in Biomaterials and Artificial Organs, 20 (1), 59-67.
Parida U.K., Nayak A.K., Binhani B.K., Nayak P.L., 2011. Synthesis and Characterization of Chitosan-Polyvinyl Alcohol Blended with Cloisite 30B for Controlled Release of the Anticancer Drug Curcumin. Journal of Biomaterials and Nanobiotechnology, 2, 414-425.
Sameer R. P., Narendra B. D., 2009. Calcium phosphate coatings for bio-implant applications: Materials, performance factors, and methodologies. Materials Science and Engineering: R: Reports, 66 (1-3), 1-70.
Schmedlen R.H., Masters K.S., West J.L., 2002. Photocrosslinkable polyvinyl alcohol hydrogels that can be modified with cell adhesion peptides for use in tissue engineering. Biomaterials, 23, 4325–4332.
Shen L., Wang Q., Wu Y., Hu X., Xie J., Junbo G., 2012. Short-term effects of fully bioabsorbable PLLA coronary stents in a porcine model, Polymer Bulletin, 68 (4), 1171–1181.
Vilaplana F., Strömberg E., Karlsson S., 2010. Environmental and resource aspects of sustainable biocomposites. Polymer Degradation and Stability, 95, 2147-2161.
Yong-Woo C., Sung-Soo H., Sohk-Won K., 2000. PVA containing chito-oligosaccharide side chain. Polymer, 41 (6), 2033–2039.
Zhao Z., Wang J., Mao H.Q., Leong K.W., 2003. Polyphosphoesters in drug and gene delivery. Advanced Drug Delivery Reviews, 55 (4), 483–499.