APPLICATION OF IONIZING RADIATION FOR SYNTHESIS, MODIFICATION & STERILIZATION OF NOVEL BIOMATERIALS AND INNOVATIVE MEDICAL DEVICES

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[ENGINEERING OF BIOMATERIALS 138 (2016) 64]

Introduction

Sterility is one of indispensable requirements for proper performance of biomaterials when utilized in medical device manufacturing. Ionizing radiation is well-established tool to sterilize medical devices and their packaging, especially in relation to their polymeric component. Beside reduction of bioburden (virtually to zero) during sterilization, radiation treatment may cause substantial changes in physicochemical properties of biomaterials. Radiation initiates essential reactions in polymers, such as polymerization, degradation, crosslinking, grafting, oxidation, etc., thus can be utilized to manufacture or modify polymeric biomaterials.

Besides studies on fundamental radiation processes, our research group led by prof. Rosiak, in the last 30 years, developed a number of radiation technologies of polymeric biomaterials [1]. Some of them have been commercialized (e.g. hydrogel wound dressings or hydrogel dosimeter for radiotherapy), some are being further modified by other laboratories and companies in Poland and abroad, while other still await industrial investments (e.g. hydrogel systems for induction of childbirth, hydrogel-based hybrid artificial organs or hydrogel-based dietary products).

Materials and Methods

Ionizing radiation facilities available at Lodz University of Technology can generate electron beams (electron accelerator) or gamma rays (^{60}Co sources), that are used to initiate radical-mediated reactions in polymers. These are water-soluble polymers, of synthetic and natural origin, typically irradiated in aqueous solution, or synthetic biodegradable polyesters, polycarbonates, their blends or copolymers. Studies on sterilization of pioneering medical devices and sterilization validation are conducted according to ISO regulations, especially of 10993 and 11137 series.

Results and Discussion

Macroscopic hydrogels, three-dimensional networks of hydrophilic polymers, found a number of practical applications in the field of biomaterials. Advantage of radiation-induced initiation for hydrogel manufacturing is avoiding any additives, as the intermolecular crosslinking reactions are initiated in a pure polymer-solvent system. [2]. Hydrogels fabricated by radiation technique can be used as 3D constructs for tissue development. For instance, gels formed by irradiation of aqueous solutions of monomers were modified with laminin [3]. Embryonic SC seeded within hydrogel scaffold were differentiated into neurons and further stimulated by microelectrode arrays exhibited neural-like tissue properties of memory acquisition and learning electrical stimulus. This may be used in pharmacological and toxicological applications to mimic neural tissue in order to reduce in vivo experiments.

Method of synthesis of nano- and micro-gels elaborated in our group (first in the world) employs high-dose-rate irradiation of dilute aqueous solution of hydrophilic polymer. Numerous radicals created at each single chain recombine intramolecularly to form crosslinked structures of single or few chains, i.e. nano- and micro-hydrogels. This method successfully competes with classical ways of manufacturing gels for application as drug carriers, chiefly because of their chemical purity [4].

Stimuli-responsive surfaces for cultivation of skin cells for treatment of large burn wounds were synthesized by radiation graft polymerization of a thermoresponsive monomer from regular cell cultivation vessels. Harvested and seeded fibroblasts proliferate to form a monolayer, which can be straightforwardly removed from the surface by reduction of temperature – the cells detach without damage, what greatly improves efficacy of the procedure – and can be transplanted onto the burn wound [5].

Radiation can cause detrimental changes in biomaterials based on biodegradable synthetic polyesters (e.g. PLA), thus incorporation of crosslinking type polycarbonate (PTMC) is beneficial for improving radiation stability of the polyester [6], and also helps adjusting mechanical properties and biodegradation kinetics. Guides for peripheral nerve regeneration require advanced biomaterial engineering, i.e. the three-step technology developed at TUL, which involves 1) manufacturing of guide tubes of PLA and PTMC blend by spraying method, 2) filling the tube with physical gel of selected polysaccharide, and after packing 3) EB irradiation [7]. Irradiation with 25 kGy causes crosslinking of the gel to form internal scaffold in the tube, moreover the implant is ready to use since sterilization is achieved simultaneously.

Sterilization method for novel biodegradable e-spun mesh, based on supramolecular polymers of ureido-pirymidinone moieties in the main-chain of polyester or polycarbonate (UPy-polymer) intended to be applied for chirurgical treatment of pelvic organ prolapse has been selected. EB irradiation is the method that guarantees sterility of entire product (SAL 10^{-6}), and the physical-chemical properties changes are acceptable when the product is packed under moisture-free protective gas.

Conclusions

Sterilization, yet the main application of ionizing radiation in biomedical field, is not the only way to exploit its potential. The other, so called 'radiation engineering of biomaterials', evolved in Poland from the technologies developed at TUL, with its applications become useful, still not widely known branch of radiation processing.

Acknowledgments

The work has been financed by the EC FP: 'Artemis' LSHM-CT-2007-037862; 'BIP-UPy' NMP-2012-LARGE-6 310389; 'Nerve Regeneration' MIGR-CT-2007-206269; by the IAEA F23028 and F23030; and by the Polish MNiSW: 3052/7.PR/13/2014/2; NCBiR 501/13-19-20-106; NCN 2012/05/N/ST5/01869.

References

[1] http://mitr.p.lodz.pl/biomat, and literature listed there.
[2] J.M. Rosiak et al., US4871490, GB2200643, DE3744289, PL151581.
[3] S. Kadlubowski et al., patent appl. P-404083.
[4] J.M. Rosiak et al., PL191664.
[5] J. Komasa et al., patent appl. P-402510.
[6] A. Adamus et al., PL222669.
[7] R.A. Wach et al., patent appl. P-409555.