BIODEGRADABLE POLYURETHANES FOR SUBSTITUTIVE MEDICINE

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Interest for synthetic bioresorbable polymers as candidates for implantable devices goes back to the early 1950. Although initially the interest was purely academic, soon first implants in the form of sutures became commercially available. Gradually, the use of bioresorbable polymers for implants broadened, primarily for drug delivery, internal fixation of bone fractures and various constructs for stapling and binding soft and hard tissues.

Over the last few years there has been increasing interest in the use of bioresorbable polymers in the design of structural scaffolds which could be used as substitutes for damaged, resected or malfunctioning tissues and internal organs. Optimally, such scaffolds implanted in place of missing tissues or organs would initiate their healing and/or regeneration. The regenerative potential of the scaffolds can be intensified by loading them with autogenous and/or synthetic growth factors or by applying "tissue engineering", i.e. seeding scaffolds with autogenous or transfected cells. The candidate polymers for scaffolds that have been investigated the most extensively over the last few years are polyhydroxyacids. Recently, new aliphatic segmented polyurethanes have been attracting increased interest. Biostable medical polyurethanes have been used for years in total artificial hearts, heart valves, intraaortic balloons, mammary implants, wound dressings, pacing leads insulation, and angioplasty balloons, to mention but a few. It has been found, however, that these polyurethanes have limited long-term molecular stability in vivo. The biologically active environment of the living organisms degrades polyurethanes, mainly through hydrolytic chain scission within ester and urethane linkages in the backbone chain and oxidative attack within polyether segments - processes which can be facilitated by the presence of enzymes and cell peroxides.

The relative molecular instability of polyurethanes may, however, be deliberately exploited in the design biodegradable materials. This can be achieved by incorporating labile moieties susceptible to hydrolysis in the polymer chain. Labile moieties are based on polyols of hydroxyacids, caprolactone, polysaccharides, aminoacids, short-chain peptides and aliphatic diisocyanates. The diisocyanates of interest are aliphatic hexamethylene diisocyanate, lysine di- or triisocyanate and tetramethylene diisocyanate. The products of degradation of these polyurethanes are biocompatible and easily metabolized. Putrescine formed upon degradation of tetramethylene diisocyanate is claimed to posses a growth factor property for various cell types. The hydrophilicity, degradation rates and mechanical properties of polyurethanes can be controlled by using specific monomers and varying synthesis conditions. Polyurethanes can be made hydrophilic, hydrophobic or amphiphilic. Their mechanicalproperties can be adjusted according to the intended application. Hydrophilic polyurethane elastomers are preferred for the preparation of implants to be used in contact with blood or as tissue adhesion barriers. Polyurethanes with higher amounts of hydrophobic component may be required for cancellous bone graft substitutes and for repair of articular cartilage. The ratio between the hydrophilic and hydrophobic components in amphiphilic polyurethanes may play an important role during contact of the material surface with blood proteins, cells and tissues. In the early eighties experi mental biodegradable polyurethanes based on lactide diols and hexamethylene diisocyanate or on mixtures of aliphatic polyurethanes with poly(L-lactide) were used for the preparation of small-caliber vascular grafts, artificial skin, esophageal and tracheal prostheses, pericardial patches and porous membranes for the treatment of periodontitis. Vascular prostheses from these polyurethanes induced in animals the growth of functional "neo-arteries". The neo-arteries had cellular structure, compliance and biological activity similar to those of the natural vessels.

Endothelial cells of the neo-artery produced prostaglandins. An "artificial skin" from biodegradable polyurethanes promoted healing of full-thickness skin wounds. Tubular microporous prostheses facilitated regeneration of resected segments of trachea and esophagus in animals.

Interest in biodegradable polyurethanes gained new momentum in the late nineties. Tubular polyurethane implants that form primary scaffolding for oriented migration of fibroblasts, Schwann cells and regenerating axons, facilitated healing of large defects in the sciatic nerve. Microporous 3-D scaffolds used as bone substitutes enhanced the regeneration of critical-size segmental long bone defects and mono-, bi- and tricortical defects in the ilium. Such defects under normal circumstances do not heal in the patient's lifetime. New attractive applications of polyurethanes would be as injectable tissue augmentation materials, injectable cements for the treatment of compression fractures of osteoporotic vertebrae and as injectable hydrogels for the replacement of calcified nucleus pulposus.

IN VIVO CHARACTERIZATION OF POLY-L/D-LACTIDE (PLDLA) 96/4 SUTURES IN THE ACHILLES TENDON OF RABBITS

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