APPLICATIONS OF POLYMERS IN CLINICAL MEDICINE

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ABSTRACT : Modern medicine would be impossible without the application of various natural or artificial materials. Among them, polymers, both natural and synthetic, play a key role. The purpose of some of them is to stay in the body forever, but others are only intended for temporary use, and, historically, these had to be removed or excreted from the body. This step can now be avoided if biodegradable materials are used; after they have served their purpose, they break down and are absorbed by the body. In medicine, biodegradable polymers offer great potential for controlled drug delivery and wound management [e.g., adhesives, sutures, and surgical meshes], for orthopaedic devices [screws, pins, and rods], and for dental applications [filler after a tooth extraction] and tissue engineering, just to name the most important. The application of biodegradable synthetic polymers started several decades ago, and since then it has been the focus of much research. This is because the requirements are quite complex: the polymer must be biocompatible, not to evoke an inflammatory response, and must have suitable mechanical and processing characteristics. Furthermore, the degradation products cannot be harmful and must be readily resorbed or excreted. For these reasons, it is important to test each material adequately before use in the human body, not only in vitro but also in vivo.
Index terms: Synthetic Polymers, Natural polymers, Biodegradable, Clinical medicine

I.INTRODUCTION

The basic principle of polymers, that is multiple assemblies of simple structural units for the formation of a 3-dimensional construct, has wide distribution in all biological systems. This ranges from intracellular filaments and cytoskeleton via structural proteins of the soft extracellular matrix and matrices with mechanical function in ligaments or cartilage to keratin of skin and hairs at the human surface interface with the environment and insects can produce silk polymers even for external constructions. Such natural polymers like horn, hair, or cellulose have been utilized by human since beginning of manhood, and they have found application in medicine, e.g. as suture material also for long time [1].

Man-made synthetic polymers are almost as manifold as the natural ones, although the most progress in development only started about in the Second World War. Newly developed polymers rapidly entered medical application, such as the polyesters and polyamides as synthetic suture materials. Synthetic polymers gained high attraction for technical as well as for medical application for various reasons. A wide range of physical and chemical properties can be achieved based on the monomer units, polymerization reaction and formation of co-polymers consisting of different components at adjustable concentrations [2]. Technologies for synthesis and formation also of complex shaped devices are mostly established. These types of polymers mainly fulfill structural and mechanical properties. Mechanical self-reinforcement is achieved by integration of oriented fibers of the same material into the matrix [3, 4]. There are also highly advanced mechanical properties, such as shape memory polymers, which can be freely deformed and return to their original shape upon a special stimulus, which can be pH, temperature, magnetic field or light. They found application in biomedicine in drug delivery devices, vascular stents, sutures, clot removal devices, for aneurysm or ductus arteriosus occlusion, and orthodontic therapy as reviewed elsewhere [5, 6]. Besides the mechanical properties also specific functional characteristics of polymers are used. Semi permeable membranes of biopolymers [cellulose] or polymers are used for hemodialysis or as drug delivery systems. Swelling or collapsing of pores of the membrane in response to pH, temperature or other stimuli leads to membranes for responsive drug release [7].

Due to their carbon based chemistry, polymers are closer to biological tissue than inorganic materials. This can be used for targeted interaction between the material and the body, but may also cause problems due to an interference of rest-monomers, degradation-products or additives with biochemical pathways. Reactive groups in the Polymers usually also offer the possibility for biofunctionalization of the surface, either because they provide reactive groups by themselves, or e.g. plasma technologies can be used to create such groups for covalent anchorage of molecules on the surface. The surface modification techniques allow independent optimization of the mechanical properties of the bulk and biocompatibility properties of the surface.

Functional types of polymers evolved for biomedical applications. Biodegradable polymers ideally stay in the body only as long as they serve their function and then they disappear without the need of a second surgical intervention [8–10]. Orthopedic fixation and ligament augmentation were the primary motivation for biodegradable polymers [11].

II. POLYMERS USED IN CLINICAL MEDICINE

Polyolefins

The polyolefins polyethylene [PE] and polypropylene [PP] are very inert and hydrophobic materials, which do not degrade in vivo. Its main application is for suture materials and meshes [12].

Polytetrafluoroethylene [PTFE]

PTFE [Teflons] has an ethylene backbone with four covalently bound fluorine molecules. It is mainly applied as vascular graft [13].

Polyvinylchloride [PVC]

PVC has an ethylene backbone with one covalently bound chlorine. Its fabrication and application requires stabilizers and plasticizers, which are the main reason for medical concerns against this polymer. Plasticizers, most frequently phthalates, turn the rigid PVC to a soft polymer, which is used for extracorporeal tubing's or blood storage bags [14].

Silicone

Silicones consist of an –Si–O– backbone with different chain lengths and crosslinks, which determine mechanical properties from liquid oil via a gel structure to rubber elastomer. There is high tolerance in ophthalmologic applications [15, 16], fibrous capsule formation at breast implants [17, 18], and synovitis as late complication in intra articular implants [19].

Methacrylates

Methyl methacrylates polymerize to very rigid polymers [PMMA] by radical polymerization and therefore find application in dentistry and in orthopedics [20, 21].

Polyesters

Biostable and biodegradable polyesters are used in biomedicine. Biostable polyesters containing aromatic groups are poly- carbonates [PC], polyethylene terephthalate] [PET, dacron]. They are used in form of membranes, filaments and meshes [22].

Polyethers

Ether bondings are biostable. Polyether ether ketone [PEEK] as hard material for orthopedic applications [23] and polyether sulfone [PES] for dialysis membranes [24].

Polyamides

Naturally, all proteins consist of units liked by amide bonds, and highly repetitive proteins like collagen or silk fibroin can be classified here. The most important synthetic polyamide with clinical application is nylon. For its high tensile strength it is used for suture materials [20].

Polyurethanes

Polyurethanes are synthesized with multiple chemistries and properties. Polyester-, polyether-, and polycarbonate- based polyurethanes with aromatic or aliphatic components are in medical use, where aromatic formulations have the better biostability [25].

III. APPLICATIONS OF POLYMERS OUTSIDE THE BODY

1. Containers

Numerous polymer devices are not inside the body, but they are used for packaging of drugs and devices. Plastic ampullas and prefilled syringes are convenient to use, but adsorption and migration of the bioactive substance into the polymer, pH shifts, oxygen permeation, optical properties and the release of leachable components have to be considered carefully for the individual applications [26, 27]. The interaction may affect not only the drug, but also the function of the polymer container. Polyolefins, HDPE or PP are the most frequent polymer for compressible vials, but frequently also multilayer containers are used to achieve required properties of inertness, oxygen- or UV protection.

2. Hemodialysis Membranes

Hemodialysis membranes are produced as bundles of hollow fibers with a blood contacting surface of 1.0–1.5 m 2. Besides the technical requirements of permeability for substances smaller than albumin and the request to prevent the passage of impurities of the dialysate into the blood, the intense blood contact poses high challenges on the blood compatibility of the membranes.

The process of removal of uremic substances during hemodialysis is controlled by diffusion along concentration gradients, pressure gradients [convection] and adsorption to the membrane. Thus, effective pore size, low membrane thickness and binding capacity for uremic substances determine the efficiency of a membrane. An especially PMMA membrane have high binding capacity for β2microglobulin or for activated complement factors and prevents their entry into circulation [21, 28].

3. Extracorporeal Membrane Oxygenation

Membranes for extracorporeal membrane oxygenation, ECMO have slightly different mode of action than dialysis membranes. In order to achieve good exchange of O_2 and CO_2 , microporous hollow fiber membranes of hydrophobic PP with pores of less than 1 μm diameter are applied [29, 30].

IV. TEMPORARY IN VIVO APPLICATIONS

1. Vascular Catheters

Vascular catheters must be non-thrombogenic and must not induce an inflammatory response in the vessel wall. Mechanical flexibility along with non-kinking and non-collapsing properties is required [25]. Central venous catheters with longer persistence in the body usually have antimicrobial fitting and properties which prevent the formation and adhesion of bacterial biofilms [31].

2. Urinary Catheters and Ureteral Stents

Urinary catheters are mostly made of latex, polyurethane or silicone. Due to a high prevalence of latex allergy and the high friction of latex, pure latex catheters are rarely used any more. General problems with urinary catheters are urinary tract infections, catheter incrustation and blockage, which also is promoted by colonization with bacteria Proteus mirabilis and damage of the mucous membrane of the urinary tract [32–34].

3. Wound Dressings

Wound dressings are a very wide field for polymers in temporary, mainly external contact with the body. Wound healing is a complex biological process, involving inflammation, clearing of cell debris, cell migration, proliferation and differentiation, and remodeling which may be disturbed at different steps in the case of delayed wound healing of chronic wounds. A wide range of synthetic, biological and hybrid materials are applied in multiple shapes to match different types of wounds [35].

V. OTHER APPLICATIONS OF POLYMERS

1. General surgical implants- Suture materials [36], Tissue adhesives and sealants [37], Surgical meshes [38].
2. Orthopedic implants - Joint prostheses [39], Osteosynthesis material [40], Bone cements [41], Scaffolds for ligament and tendon repair [42]
3. Vascular and cardio-vascular intervention - Vascular stents [43], vascular grafts [44].
4. Plastic, reconstructive and cosmetic surgery – [45].
5. Ophthalmology - Contact lenses [46], intraocular lenses [47], and other polymer devices in ophthalmology [48].
6. Dentistry – Composites [49]

VI CONCLUSION

Numerous types of polymers are currently in use in virtually all fields of medicine. The different polymer classes with tailored formulations like adjusted molecular weight, cross- linking degree, degree of crystallization, co-polymers and blends and additional bioactive surface functionalization allow this wide range of applications. While engineering-related properties like stiffness, tensile stability and elasticity are usually primary characteristics for selecting a polymer, also toxicity and biocompatibility aspects have to be taken into account. Biodegradation as a more advanced property of some polymers finds application in an increasing number of fields from suture materials via orthopedic stabilizing materials to vascular stents, because these devices may disappear after they fulfilled their function. These are the imitations of natural products. They are going fulfill the natural products should soon appear on the medical device market in future.

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