Recent Progress on the Science of Biomedical Polymeric Materials

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Abstract
The science of biomedical polymeric materials has become of interest in recent years. The review concerns particularly on the biomedical polymeric materials that have been developed, especially focussed on those of contact lenses, dental polymers, adsorbable sutures, artificial skin, liver, kidney, heart and so on. The problems for their use are discussed.

KEY WORDS: (Biomedical Polymer) (Contact Lense) (Dental Polymer) (Adsorbable Suture) (Artificial Organ)

1. Introduction

In recent years, the science and technology of preparing and applying plastic materials in the biomedical field have received much attention. Interest in utilizing both natural and synthetic polymeric materials, especially in such a field is increasing rapidly.

In this review, emphasis is focussed particularly on the biomedical polymers that have been fully developed. The content of the present review is classified as follows:

a. Biomedical polymeric materials that have little contact with blood and are used primarily as supplementary material, such as contact lenses, dental polymers, adsorbable sutures, and artificial skin.
b. Materials that are in contact with blood but only for a short time, such as artificial red blood cells, artificial liver, artificial kidney, and artificial lung membranes.
c. Materials that are in contact with blood for a long time or permanently, such as heart valves and shunts. The artificial heart may be included in the latter category.

Several reviews have been published (ref.1-7) in these areas and should be referred to for further information.

2. Contact Lenses

Presently about ten million people worldwide wear plastic contact lenses. The optical advantage of contact lenses over the usual ones is considerable. The latter alter rays of light before they reach the eye, whereas contact lenses make the optical correction on the surface of the eye. Contact lenses simulate the normal eye by directing the rays to the retina.

Contact lens development was very rapid following World War II with the availability of methacrylic resin. The pioneering work of Wichterle and Lim in the late 1950s using acrylic-type hydrogels opened the way for soft contact lenses, which have completely revolutionized the industry.

The materials used for contact lenses should be (a) optically transparent, (b) permeable to oxygen, (c) physiologically inert, and (d) mechanically stable. It appears to be relatively easy to find polymeric materials that have good transmittance of light and a refractive index close to that of the cornea: 1.37. Major problems arise when we look for materials that is permeable to atmospheric oxygen, because the cornea needs oxygen for the metabolic processes of its living cells. The lenses should be physiologically inert and afford minimal disturbance to the cornea and surrounding eye tissues. This implies that the lenses should be finished absolutely free of impurities.

Two types of the polymers are currently being used as materials for contact lenses: thermoplastics and hydrogels. The thermoplastic materials are generally hard and hydrophobic; the hydrogels are soft and hydrophillic.

Most hard contact lenses are made from methacrylic resin, which is the mainstay materila because of its optical properties, toughness, and physiological inertness. Most hard lenses are crosslinked with other monomer to improve their strength, hardness, and scratch resistance. The most serious drawbacks of hard contact lenses are their hydrophobic property and resultant low permeability to oxygen.

Soft contact lenses are usually manufactured from acrylic hydrogels, which are derived from slightly crosslinked poly(2-hydroxyethyl methacrylate)(abbreviated as HEMA). The fundamental property of a hydrogel is its equilibrium water content, by which the permeation of oxygen through the hydrogel is substantially facilitated.

3. Dental Polymers

Most people develop caries of the teeth. In some diseases the teeth are lost, and as they do not regenerate naturally, artificial materials must be used as a replacement. In addition, synthetic polymers play an important role in curing caries and can also serve as effective materials for the prevention of caries.

To develop materials for dental uses, the following properties are necessary: (a) chemical stability, (b) mechanical strength, (c) biocompatibility, and (d) good adhesive property to teeth. Since dental materials used as fillings remain in the mouth for the long time, they should not be degraded by the action of saliva, microorganisms, or food. Furthermore, they should not wear out under strong repetitive occlusal stresses. The polymerization of monomers must proceed in the mouth under biologically mild temperature in an excess amount of water on and in the tissues. The heat of polymerization must be low to avoid damage to the surrounding tissues. It should also be noted that shrinkage must be limited because any space between the teeth and the filling materials form an ideal place for further caries to develop.

Although methacrylic polymer has a wide application as a dental material, it has a serious defect in that it does not adhere substantially to tooth surfaces. As is well known, polymer dental fillings often fall out. Furthermore, the poor interface contributes significantly to secondary caries because of the percolation of microorganisms, liquids, and other materials into the marginal areas of the restoration.

An effective way to overcome this drawback is to develop adhesive dental filling materials. One approach is an acid stching of enamel to effect a mechanical interlock. Another is the application of functional monomers that could chelate with calcium ions or couple with dentine collagen. Recently, it was found that the monomers having both hydrophilic and hydrophobic groups have good adhesion property for tooth tissue.

4. Adsorbable Sutures

Special fibers are required for suturing body parts such as skin, muscle, and blood vessels together after an operation or an accidental cut. Many sutures are required to be degradable and absorbable since they remain in the body after the operation. Polyglycolic acid was designed as an artificial surgical suture which combines many of the factors necessary for a suitable biodegradable implant. Sutures are considered to be the first successful example of made-to-order biomedical polymers.

The characteristics required for an acceptable biodegradable suture are as follows: formability, adequate initial strength and dimensional stability, controlled rate of strength loss, complete absorbability, low order of toxicity of both implant and degradation products, and sterlizability. A combination of these unique properties is necessary to produce a useful biodegradable system.

5. Artificial Skin

The most important function of the skin is simply as a bag to contain our body parts and fluids. The skin protects these parts from drying out and constitutes our first line of defense against microbial invasion. Both excretory and secretory glands contained in this complex organ are used to regulate the body's fats, water, and electrolytes. Our skin is also the organ for the reception of thermal, tactile,and painful stimuli.

Artificial skin made of synthetic polymers should satisfy the following requirements:

1. It should control the amount of loss of body fluids, protein salt, or heat from the wound surface.
2. It should protect against a variety of infections.
3. It should promote the formation of granulation and epithelium.

Biomaterials such as autografts, cadaver skin, or pig skin find a wide application to current treatment for fluid resuscitation and prompt covering of wounds. In addition to these materials, collagen, the main component of the skin, takes advantage from the viewpoint of biocompatibility. Natural collagen can be regenerated enzymatically and chemically in the form of a membrane, sponge, or unwoven cloth.

Although the application of many synthetic polymeric materials, such as nylon and Dacron, were studied, a single material did not satisfy the number of requisites for artificial skin. Consequently, multiphase polymers of laminate type have been found to be applicable for this use. Laminated polymers made of polyurethane-collagen or silicone-nylon system have also been explored.

More recently, Yannas's group has developed a successful artificial skin for practical use. The skin in question consists of a bilayer polymeric membrane made of silicone and biodegradable protein layers. Assuming that the assimilation of the artificial skin with the natural skin, the use of epidermal cells of patients themselves may afford a promising way to prepare a well-designed artificial skin in the future.

6. Artificial Red Blood Cells

Several attempts have been made to prepare artificial red blood cells by making use of microencapsulation technique. The ideal is to be able to make blood transfusions independent of blood type and without any infection.

Microcapsules made of collodion, nylon, and dextran stearate have been developed. However, none of these materials survived for a long time in the cieculation system after injection into the blood. In addition, it is necessary for the artificial red blood cells to be less than 0.5 micrometer in size with high deformability in order to pass freely through capillary blood vessels.

In recent years, promising artificial red blood cells have been prepared using an interfacial polycondensation technique. These cells are hemoglobin-loaded microcapsules that are negatively charged and are similar in size and deformability to those of natural red blood cells. It is expected that these synthetic cells are practical enough to use with respect to the absorbability of oxygen, and enzymatic activity and fluidity.

7. Artificial Liver

Activated charcoal has excellent adsorbability for many organic molecules. It can, therefore, be used as an artificial liver for adsorption-type impurities, with the main purpose of removing metabolic materials that the body excretes. It is particularly effective for the removal of poisons, drugs, and drug metabolites introduced in toxic excess in the body.

Direct use of activated charcoal as artificial liver resulted in failure because of the release of activated charcoal microparticles which have no blood compatibility. These caused a blockade of capillary blood cells by thrombocytopenia. To overcome these drawbacks, encapsulated activated charcoal has been developed. For example, coconut and pitch-base spherical activated charcoal particles were coated with gelatin, collodion, or HEMA polymer. This pitch-base spherical encapsulated activated charcoal is a promising adsorbent for metabolites and poisons and is being reaied for clinical trials.

8. Artificial Kidney

In 1960, dialysis began to be used in the medical field as a substitute for the human kidney. The blood of patients suffering from renal poisoning is purified by passing it through cellulosic membranes against a dialysate. Subsequent development of small semipermeable hollow fibers provided the basis for the design of small, efficient commercial dialyzers. The blood to be purified is passed through the inside of the hollow fibers, while the dialysate is distributed over the outside. Metabolic wastes, such as urea, uric acid, and creatine, rapidly diffuse from the blood through the membrane and into the dialysate.

In addition to the dialysis, blood ultrafiltration affords an effective method for separating middle-molecular-weight components in blood. The requisites for the membrane for the purpose of artificial kidney are that:

1. The membrane have an appropriate channel diameter for dialysis and ultrafiltration.
2. The essential components of blood not be adsorbed or converted.
3. Blood clotting should not occur.
4. Convenient sterlization must be possible and toxic components should not solute out.

The first material used for the artificial kidney in the cure of an acute renal insufficiency was cellulose. This material still finds extensive use in the cure of chronic conditions. Other synthetic materials have also been found to be efficient membranes for this purpose.

Regenerated cuprammonium cellulose, called cuprophane, has the greatest usage in the world. It has good mechanical strength, which enables the manufacture of thinner cellulose membranes. The thickness of the membrane is 6 micrometer, which is 20 micrometer less than that of the original membrane. This results in improved filtration rates and permeability of middle-molecular-weight components.

Simple membranes made of methacrylate polymers cannot satisfy solute permeability and the mechanical strength requirements simultaneously. However, suitable membranes can be produced for blood dialysis with excellent properties when a mixture of isotactic and syndiotactic methyl methacrylate polymers is used. The original membrane performs well for blood ultrafiltration, but the modified membrane is applicable to the blood dialysis.

Other synthetic membranes made of polyacrylonitrile or ehtylene-vinyl alcohol copolymer are also being used commercially.

9. Artificial Lung Membranes

The artificial lung is a prosthetic device presently used in an extracorporeal blood circuit for partial or total gas exchange during cardiac surgery. Besides ability for gas exchange the requirements for the materials and the apparatus for an artificial lung are that the treatment and management are as simple as possible, that complete sterilization can be performed, and that damage to the blood during use is negligible. Therefore, it is recognized that disposable materials are most desired.

The artificial lungs used now are classified principally into three types:

1. The bubble oxygenator. Gas exchange is carried out by bubbling oxygen gas in a finely distributed form through the blood. The structure of the apparatus as well as the treatment is simple and the materials are disposable. However, blood foams when stirred with oxygen, causing severe problems, thus making it necessary to provide defoaming equipmemt.
2. The film-type oxgenator. In this case, the blood comes in contact with oxygen gas as it passes over an array of films, a process that allows for gas exchange. In comparison with the bubble oxygenator, the damage to the blood during the process is much lower; however, this oxygenator is not disposable and the cleaning, sterilization, and reconstruction are inconvenient.
3. The membrane oxygenator. Using polymeric membranes with high gas permeability, gas exchange tkaes place in the blood. This gentle process minimizes the progressive destruction of blood cells and denaturation of plasma proteins compared with other types of oxygenators.

The membrane used for the artificial lung was first made of Teflon, because of its availability in thin sheets to produce large areas and its fair blood compatibility. During the early 1960s, thin membranes of silica-filled silicone rubber were developed. Silicon rubber has the highest specific gas permeability, and pure filler-free silicone rubber has been shown to minimize thrombosis and platelet sequestration. Presently, membrane lungs are also being prepared from porous polypropylene, Teflon, and silicon-cellulose, which have extremely high gas permeabilities.

10. Artificial Heart

In recent years the fabrication of a number of implantable cardiovascular devices using synthetic polymers has received much attention. Rigid polymers have a variety of applications in the fabrication of implantable blood pump housings, as blood-contacting components used in valves, and as connectors to couple biologic tissue to the blood pump. A variety of rigid polymers are now available; however, each has certain disadvantages.

The first study on the fabrication of implantable cardiovascular devices was begun by Kolff and Akutsu in 1958. In parallel with the active research in USA, Atsumi and his group developed new devices independently in Japan. Of all the systems concerned with the development of an artificial heart, the most important one is the blood pump. It is recognized that the development of special polymeric materials suitable for the blood pump is essential. The important properties that these polymeric materials should possess are durability, processability, and antithrombogenity. Studies to produce more desiable polymeric materials are still going on.

The materials now available can be classified in two groups. The first group are the synthetic polymers that have smooth surfaces, such as silicone rubber, polyurethane (Biomer and its copolymer, Cardiothane) and polyvinyl chloride paste; the second group are the biological and modified biological materials.

Several elastomeric materials have been evaluated for the fabrication of prosthetic blood pumps. One is a type of segmented polyurethane, the chemical structure of which is similar to that of Biomer, although the mechanical properties are apparently inferior. The others, Cardiothanes, are said to be copolymers of polyurethane and silicone rubber. This material is siutable for intravascular use and has been used in the fabrication of the intra-aortic balloon pump (IABP). The fabrication techniques are more difficult than those for Biomer. Atsumi, Imachi and their groups in Japan, have produced a new blood pump material by covering a polyvinyl chloride pump body with Cardiothane so that properties such as durability and processability were greatly improved.

As other hard materials, both artificial bones and teeth should also be reviewed.

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