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Past, Present and Future Role of Polyurethanes for Surgical Implants

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Abstract - Polyurethanes, which were once thought to be unstable when used in the body, are now occupying a dominant place in the armamentarium of the biomedical researcher. This paper discusses the history of this class of biomaterials, its chemical structure relevant to long-term surgical implants, physiological acceptability based on standard animal tests, the effects of some modifications, and possible areas of future developments with promising but yet untested formulations.

INTRODUCTION

Polyurethanes are a diverse family of polymers capable of exhibiting a wide range of properties depending upon their molecular composition. Generally, they consist of isocyanate and glycol portions in the presence of a variety of chemical entities that are isocyanate-derived during polyurethane preparation. With the exception, perhaps, of the fiber-forming varieties, these compounds contain numerous non-urethane bonds tied into their polymer structure. Two of the most frequently used building blocks are polyether and polyester polyols to form related linkages that significantly determine performance. Some twenty years ago, *polyester*-derived polyurethanes were considered for medical applications. Unfortunately, at that time, there was no clear understanding of *in vivo* performance between the basic forms. Consequently, this early experience resulted in rapid hydrolytic degradation of polyester polyurethane implanted in laboratory animals. Despite its high strength, abrasion resistance, flexual endurance, and practical handling characteristics, the material was essentiallly abandoned.

In 1966, it was realized that specific *polyether* urethanes were hydrolytically stable *in vivo* and suitable candidates for long-term surgical implants (1, 2). Subsequent studies have investigated aspects of tissue response, chemical biodegradation, blood compatibility, as well as hydrolytic stability (3, 4). Medical applications which have benefited as a result of these findings are aortic grafts, vascular tubing, endotracheal tubes, heart assist devices, pacemaker wire insulation, heart valves, transcutaneous access sets, catheters, restorative and preventative dental materials, components of hemodialysis units and others. Some work indicated that *in vivo* performance could be improved by modifying the surface in various ways such as using additives or coverings of textile fibers (5). However, actual experience has shown that these alterations are only selectively advantageous for specific applications. Performance within the vascular system is judged best when a smooth, uninterrupted or uniformly textured surface is presented to the blood. Numerous new formulations are in the early stages of development and promise opportunities for a wider choice of properties.

DISCUSSION

Chemical Structure

The realization that specific chemical structures of the polyurethanes influenced, to varying degrees, hydrolytic stability when implanted subcutaneously was a major reason for the re-establishment of polyurethanes as surgical implant materials. Three-year implants in dogs (6) showed that significant differences existed between polyester and polyether polyurethanes, with the latter showing no physical changes over that time period. Segmented polyurethane (Lycra® spandex polymer T-126*) was the first of this more stable group to be recognized (1, 2) and adapted to medical needs. Figure 1 shows the essential difference in structure between the two basic types. The use of this polyether polyurethane has grown until today it ranks high among the list of those elastomeric materials most suitable for use within the body. Several other polyurethanes of slightly different chemical composition have subsequently shown promise.

*Dupont polymer T-126. Now available as Biomer from Ethicon Inc., Sommerville, NJ.

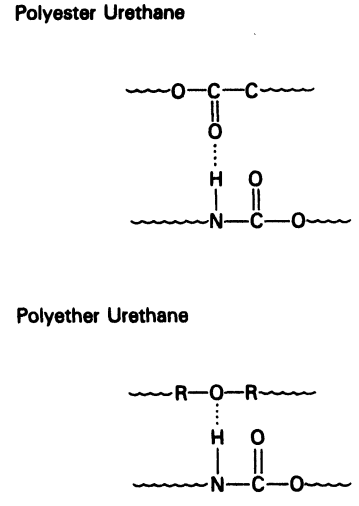

Fig. 1. Structural differences between polyester and polyether urethanes.

For biomedical investigations, polyurethanes have been mostly based on the 4, 4' diphenylmethane diisocyanate (MDI) prepolymer rather than the conventional toluene diisocyanate (TDI) prepolymer (see Fig. 2). MDI offers less of a health hazard to workers dealing with the raw materials based on their vapor pressure differences (MDI; 0.0075 mm Hg, TDI; 1.9 mm Hg @ 200°F) which can pose a potential inhalation risk to breathing toxic vapors (i.e. free isocyanate). Exposure limits as set by the NIOSH are 0.005 parts per million in air for an 8-hour time weighted average, and 0.02 ppm for a 20-minute exposure period. Further, MDI systems can generally be approved by the FDA for packaging and processing of dry foods. MDI compounds generally excel, in resilience, abrasion resistance and hydrolytic stability. However, there is some concern as to whether by-products of MDI can produce mutagenic effects as implants (8).

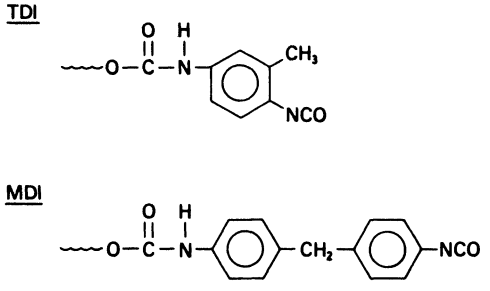

Fig. 2. Structural differences between toluene diisocyanate (TDI) and 4, 4' diphenylmethane diisocyanate (MDI).

Burpee and coworkers (9) found that amine-cured polyurethanes were more stable and tissue compatible than glycol-cured polyurethanes. Although both kinds are now being used, consideration as to the merits of each add another order of complexity to the array of choices offered by this versatile class of polymers.

Polyurethanes Under Evaluation for Medical Use

Currently there are several polyurethanes on the market that are being considered for medical applications: Biomer®, Tecoflex HR®, Pellethane Series 2363, Texin® Medical Polyurethane, Bioelectric polyurethane and Avcothane® copolymer. Each is reported to have distinct advantages. Some are thermoplastic in nature while others are not, but all are derived, at least in part, from polyethers.

Tecoflex HR®: Tradename, Thermoelectron Research Corp.
Pellethane®: Tradename, The Upjohn Company.
Texin®: Tradename, Mobay Chemical Company

The most widely used groups are the segmented polyurethanes which are elastomeric block copolymers consisting of hard crystalline segments dispersed between flexible amorphous segments. The flexible segments provide elastic recovery properties to the polymer whereas the hard segments provide sites for intermolecular secondary bonding. The tensile properties of the system can be varied depending upon the degree of this intermolecular bonding which also influence the thermoplastic nature of the material.

Biomer® is a polyether segmented elastomer consisting of hard segments of urea and soft segments of polyether glycol crosslinked by urethane. It possesses a high modulus of elasticity, physiological acceptability, resistance to flex-fatigue and excellent stability over long implant periods. The molecular arrangement is based on the original formulation from which Lycra® spandex fibers are produced. Its structure consists of two segments, one which is crystalline in nature and represents one or more repeating units of a urea polymer derived from an amine and the other segment which is a polyether glycol chemically bonded to the first. Since the final material is synthesized from a urea and a polyether glycol linked by urethane groups, they are polyether/urethane/ureas or otherwise known as segmented polyurethanes (10). A solution of the polymer is the most common, and devices are usually fabricated by repeated dipping or coating. The chemical structure of this polymer as suggested by Lee and associates (11) is given in Fig. 3.

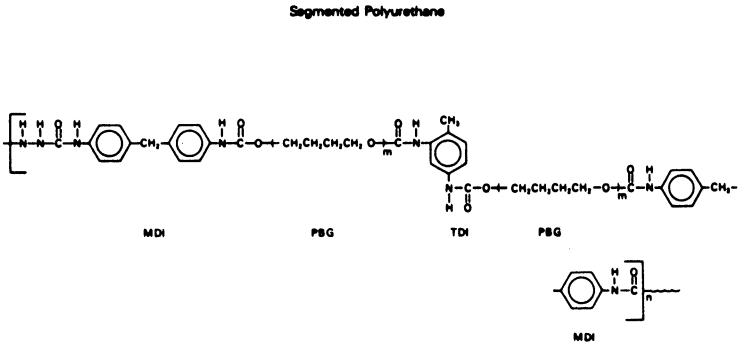

Fig. 3. Structural configuration of a segmented polyurethane (Lycra T-126).

Szycher and associates (12) have developed an aliphatic, polyether-based, linear segmented polyurethane containing 100-percent urethane linkages in the molecular backbone. The polymer is Tecoflex HR® and can be molded by casting successive layers or can be processed from a reactive two component system that is heat cured. The polymer is reported to withstand flexing of 80 x 10^6 cycles for two years as a cardiac assist pump diaphram. Acute toxicity tests investigated by Szycher showed "no adverse reactions . . . and the kinetic clotting index was found to be approximately equal to other biomedical urethanes".

Several thermoplastic polyurethanes that are invaluable for extruding and injection molding are being considered for medical products and devices. They are based on polytetramethylene ether glycol carrying a series of hardnesses from relatively soft--Shore A80 to almost rigid--Shore D70. Pellethane® and Texin® are typical. Pellethane® is a polyether material that exhibits hydrolytically stable characteristics (13). For example, physical properties are relatively unchanged after 30 days exposure at 70°C and 100-percent relative humidity for the 2363 series. Texin® is also polyester based and available in two hardnesses (MD85: Shore A85 and MD90A: Shore A90). Both polymers have passed Class VI tests of the U.S. Pharmacopea tests for acceptable pyrogen levels and tissue culture tests for cytopathic effects (14, 15). *In vitro* toxicity tests, generally, have shown them to be relatively inert and may be suitable for short-term and possible long-term subcutaneous applications. Figure 4 shows the generalized form of thermoplastic polyurethanes as opposed to those which are crosslinked.

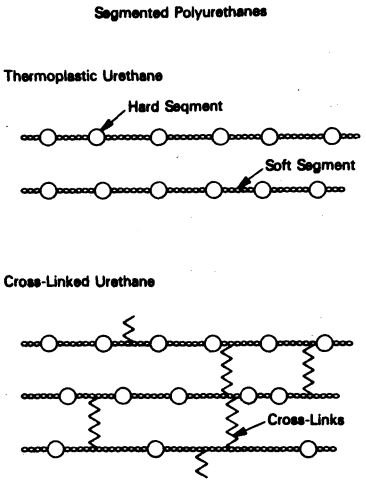

Fig. 4. Generalized form of thermoplastic and cross-linked urethanes.

Sharp and associates (5) introduced a carbon-filled polyurethane in solvent form as a possible non-thrombogenic coating for textile materials to be used as vascular grafts and artificial heart diaphrams. The formulation, although proprietary, is based on a diamine-cured polyurethane with 10-percent carbon black added and is applied by dipping or coating. Sharp reports that the surface possesses a strong negative charge and coupled with the excess of amine that is present in their compounds seems to account for much of its success as implants in their experimental animals.

Avcothane® is a polyurethane/polysiloxane block copolymer that has been used clinically as balloon heart assist devices with thousands of patients. The composition is proprietary in nature. Careful control over the handling of the liquid polymer during film-making is essential since the siloxane-urethane material can be relatively thrombogenic or nonthrombogenic depending upon whether the blood comes in contact with the side that was cast against the mold or the air side. According to Nyilas, this is especially true if siloxane groups are dominant at the blood/polymer interface (16).

Physical Considerations

Processing conditions can have a great influence on the properties and behavior of some polyurethanes. For example, Wilkes and associates (17) found that for polyester urethanes, sudden thermal changes can cause microphase separation to the extent that physical properties which otherwise would be similar to those of polyether materials are significantly reduced in value. Optimum thermal treatment is time-dependent and is best accomplished through an annealing sequence.

Composition can play an important role in the life expectancy of some surgical implants. Lyman and coworkers (18) coated a dacron knit tube with polyurethane in such a manner as to closely mimic the physical characteristics of blood vessels. These vascular grafts were reported to show improved patency as a result of closely matching the graft's compliance with that of the natural vessel. Further, an increase in porosity based on this construction also added to its improved performance.

Infection was believed to be reduced in transcutaneous devices studied by Annis and associates (19) because of the construction of a microfibrous non-woven fabric cuffs which allowed tissue ingrowth into the device. Microscopic examination showed that tissue attachment was so close that it offered an effective barrier to infection.

The Future of Polyurethanes

As experience grows, carefully selected polyurethanes are being used in greater amounts for surgical implants. Medical industry and other research groups are finding a wide range of properties available and developing efficient means of modifying and fabricating various compositions to achieve exacting requirements. By applying the appropriate chemical combinations, an end product may be achieved having appropriate tissue compatibility, physical

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Avcothane®: Tradename, Avco-Everett Corp.

endurance and sophisticated design capabilities for a host of applications. New compositions are being devised for innovative use such as controlled drug release, vascular grafts, artificial heart prostheses, transcutaneous access devices and a variety of novel catheters. Polyurethane based hydrogels are being investigated as coatings and fillers for increased compatibility of other polymer systems. Polyurethanes may well add to our knowledge of the lipid absorption and calcium deposition problems observed in and on polymers by providing a means of determining uptake as a function of polymer variations. Through its myriad chemical possibilities it may be possible to achieve a better understanding of platelet adhesion, activation, and release mechanisms, the thermodynamic nature of plasma protein adsorption, and confirmation of surface free energy theory as it relates to biocompatibility. Undoubtedly, urethane technology for biomedicine will continue since the chemical components available for development of ordered systems are numerous and the versatility of the polymers so enormous that they are limited only by the imagination and resourcefulness of the researcher.

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