Segmented polyurethanes and polyurethaneureas are the materials of choice for a broad range of implantable and extracorporeal biomedical devices. They are the reaction products of hydroxyl-terminated polymer oligomers, chain-extending, low molecular weight diols or diamines and isocyanates. The latter may be aliphatic, cycloaliphatic or aromatic.

The majority of "biomedical" polyurethanes and polyurethaneureas are synthesized from the aromatic disiocyanate diphenylmethane-4,4'-diisocyanate (MDI). Of the commercially available disiocyanates, MDI gives the best combination of physical/mechanical properties in thermoplastic formulations and in the spandex elastomers such as Biomer® and Lycra®. In the later the thermodynamic incompatibility of the MDI/ethylene diamine hard segment with the polyester soft segment is thought to be responsible for the extremely low hysteresis behavior and excellent flex life of this class of elastomers relative to aliphatic and cycloaliphatic polyurethane.

Long flex life is a first order requirement for candidate elastomers in applications like circulatory assist devices, vascular grafts, pacemaker leads and similar biomedical applications. Material failure in these devices can result in immediate and potentially fatal consequences to the device user. Recently there has been increased concern regarding the release of potentially carcinogenic by-products from MDI-based polyurethanes. The formation of urethane from an isocyanate and a hydroxyl is an equilibrium reaction. As temperature is raised urethane groups dissociate back to the hydroxyl and the isocyanate. This process occurs in all polyurethanes during extrusion and molding. Urethane bond reformation is partially responsible for the time-dependence of physical properties seen following melt processing.

If water is present when urethane groups dissociate, it can react with free (di)isocyanate to form the corresponding amine. In the case of the aromatic isocyanates, the hydrolysis product is an aromatic amine or aniline compound, several of which give positive results in the Ames test. The mutagenicity of the corresponding cycloaliphatic diamines is unknown at this time.

Practical considerations require that the polyurethane thermoplastics be processed in the absence of water. Extrusion or molding polyurethanes in the presence of water generates CO2 in the same reaction which forms free amines. Even a small amount of CO2 generation produces obvious bubbles and surface defects in the configured product and is easily detectable. Most biomedical devices are used below 40°C. In this temperature range there is no evidence that urethane dissociation occurs at any detectable rate. The only other set of conditions which might be encountered by a device that could result in amine formation are those used in steam sterilization. Manufacturers of biomedical urethanes recommend against steam sterilization for this reason. The 120°C temperature used in the typical autoclave cycle is sufficient to dissociate urethane bonds and the abundance of ambient water definitely can lead to amine formation. However, for thermoplastic polyurethanes these same conditions produce gross and permanent distortion in the configured part, leaving no doubt about its thermal history. Proper handling and processing of aromatic thermoplastic polyurethanes can effectively prevent the formation of aromatic amines. In reproducing the work of Ulrich and Bonk in our laboratory we could detect no methylene diamine (MDA) in MDI-based urethanes extruded at standard processing conditions. We do, however, see the need to standardize a sensitive and rapid analytical method capable of detecting MDA in the ppb range. Of the several methods we have evaluated to date, an LC method involving derivatization and a thin layer chromatographic technique appear to be the most sensitive.

A procedure used by Syzch et. al. begins with a choroform extraction step of the solid polymer. The extraction, done at reflux temperatures, is itself capable of inducing degradation in some polyurethanes. When subjected to this process the aliphatic polyetherurethane, Tecoflex®, was completely solubilized and badly discolored.

Reliable test methods for polyurethane degradation products can supplement molecular weight measurements by GPC in the development of polyurethanes with increased thermal/hydrolytic stability. Because autoclaving is such a severe test for this property, we use it as an accelerated test method to evaluate structure/thermal stability relationships in polyurethaneureas. We have found that the most thermally unstable portion of the polyurethanes based on poly(tetrahydrofuran) glycols is this polyester soft segment, not the hard segment containing the disiocyanate residue. Degradation causes molecular weight reduction with little effect on the polydispersity of the molecular weight distribution. Multiple autoclave cycles causes reduction in tensile strength and an increase in ultimate elongation. With changes in structure and stabilization we have prepared polyurethanes which actually increase in molecular weight and strength through several autoclave cycles. The evolution of (toxic) decomposition products such as tetrahydrofuran monomer in these modified materials is reduced concomitantly.

Tecoflex®, Pelthane®, Biomer®, Cardiothane® and the majority of polyurethanes of interest biomedically, are synthesized from poly(tetrahydrofuran) glycols. Before any subset of this useful class of materials is condemned for its tendency to produce toxic decomposition products, we should better understand the similarities and real differences which exist among them.

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