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New biomedical polyurethane ureas with high tear strengths

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Summary

Biodegradable polyurethanes ureas (PUU) were synthesized by a two step polymerization. First a poly (ε-caprolactone) prepolymer was terminated with three different diisocyanates: lysinediisocyanate (LDI), 1,6-hexanediisocyanate (HDI) and 1,4-butanediisocyanate (BDI). Second the prepolymers were chain extended with 1,4-butanediamine. The degradation products of these polymers are non-toxic. The mechanical properties of the PUU are compared with those of three PU's. Compared to these PU's, the HDI and BDI based PUU showed a very high resistance to tearing.

Introduction

Polyurethanes are widely used as elastomeric biomaterials because of the excellent mechanical properties and the good blood biocompatibility (1). Examples of applications are veins (2-4), nerve guides (5), artificial skin (6) and meniscal reconstruction material (7,8). However, segmented medical grade polyurethanes like Estane, Pellethane, Biomer and Mitrathane contain aromatic diphenylmethane diisocyanate (MDI) in the hard segments. It has been shown that upon processing, sterilization and degradation the carcinogenic methylenedianiline is formed and released (9-10). A new medical grade polyurethane, without these side effect is highly desirable.

In this study polyesterurethane ureas (PUU's) based upon hard segments, which will release non-toxic degradation products, and a poly(ε-caprolactone) soft segment were synthesized. Diisocyanate terminated prepolymers were chain extended with 1,4-Butanediamine. This substance, also known as putrescine is essential for cell division in mammals. The hard segments were varied by using three diisocyanates: lysinediisocyanate (LDI), 1,6-hexane diisocyanate (HDI) and 1,4-butane diisocyanate (BDI). Upon degradation these components will release L- lysine, hexanediamine and 1,4-butanediamine, respectively. The thermal properties are described and mechanical properties of the PUU's are compared to those of three PU's.

Experimental

Materials: Poly(ε-caprolactone) diol (Mw=2000, Aldrich) was azeotropically dried with toluene. The synthesis of ethyl 2,6-diisocyanatohexanoate (L-lysine-ethylester-diisocyanate LDI) has been described elsewhere (12). 1,4-Butane diisocyante (Aldrich and DSM), 1,6-hexane diisocyante (Merrck-Schuchard), LDI, 1,4-butanediamine (BDA) and N,N'-dimethylformamide (DMF, Janssen Chimica) were distilled prior to use. Estane 5701-F1 was obtained from B.F. Goodrich Chemical Co. Elate 108 prepolymer was obtained from Akzo Nobel.

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Polymerization: Diisocyanate terminated prepolymers were prepared by reacting of the hydroxyl terminated poly(ε-caprolactone) in a six fold excess of BDI, HDI or LDI at 80°C for four hours. The excess diisocyanate was removed under reduced pressure (0.01 mBar) in a Kügelrohr at 70°C. For chain extension, the prepolymer was dissolved in DMF (6 wt.-%) and a dilute solution of BDA in DMF (1.4 wt.-%) was added slowly at room temperature. Synthesis of linear Elate and Elate network was described elsewhere (8).

Polymer processing: The synthesized PUU were purified and freed from unreacted monomer and low molecular weight material by precipitating DMF solutions in isopropylalcohol. Films were prepared by casting hot PUU solutions of 160 °C in DMF (3%) at 50°C. Estane 5701-F1 films were prepared by casting 1,4-dioxane solutions. The preparation of Elate films was described elsewhere (8).

Polymer characterization: Intrinsic viscosity of polymers was measured in m-cresol at 25°C using an Ubbelohde viscosimeter. Dynamic mechanical analysis was performed using a Rheometrics RSA-II DMTA. In tension mode at a constant loading, films (0.35 x 3 x 35 mm^3) were subjected to an oscillating strain of maximal amplitude of 0.5% at a frequency of 1 Hz. Heating rate was 5 °C/min. Tensile testing was performed on rectangular-shaped specimens (40 x 0.75 x 0.35 mm), cut from thin films at room temperature using an Instron (4301) tensile tester, equipped with a 100 N load-cell, at a cross-head speed of 10 mm/min. For tearing experiments, trouser specimens of 3.75 long, 1.25 cm wide and a longitudinal slit of 2.5 cm were used. The thickness of the test piece was 0.33 $\pm$ 0.04 mm. During testing the force was applied normally to the plane, operating a crosshead speed of 250 mm/min (ASTM D 1938-62T).

Results and discussion

Polymers

The PUU's were synthesized by chain extending a diisocyanate terminated poly(ε-caprolactone) (PCL) prepolymer with 1,4-butanediamine (BDA). For the synthesis of the prepolymer, PCL diol was dissolved in a six fold excess of BDI, HDI or LDI. The excess was used to limit the formation of PCL dimers, trimers etc. Afterwards the excess was removed under reduced pressure. This way, PUU's could be synthesized reproducibly. L-Lysine-ethylester-diisocyante (LDI) was used because of its non-toxic degradation product L-lysine. 1,4-Butane diisocyanate (BDI) was used because it will yield 1,4-butanediamine upon degradation, also known as putrescine, which is present in cells of mammals. Additionally, BDI is expected to form good hard blocks with the chain extender. Hexamethylene diisocyanate (HDI) was used, to observe changes of properties by small change of hard blocks. The intrinsic viscosities are presented in table 1.

Thermal properties

Since the mechanical properties of polymer are largely influenced by their morphology, the thermal properties of the polymers were investigated. DSC thermograms of PUU films are shown in figure 1. The DSC scan of the LDI based PUU exhibit a Tg at -52.1°C and two melting endotherms at 40.5°C and 90.9°C with respectively melting enthalpies of 15.9 J/g and 11.5 J/g. The Tg and lower melting temperature correspond to

Table 1

	intrinsic viscosity (dl/g)
LDI based PUU	2.18
BDI based PUU	1.05
HDI based PUU	1.72

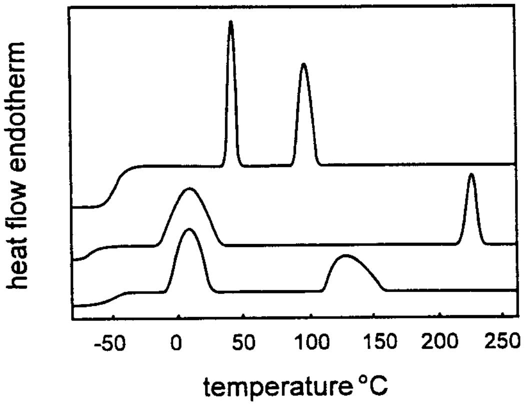

Figure 1. *DSC-curves of a: L-lysinediisocyanate base PUU, b: butanediisocyanate based PUU and c: hexanediisocyanate based PUU.*

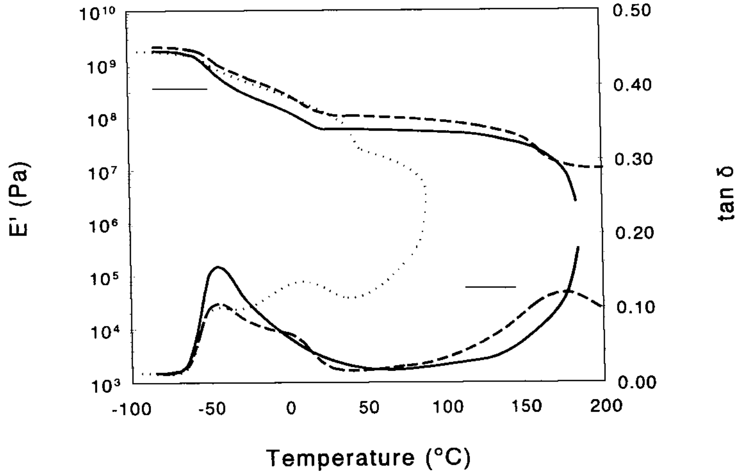

Figure 2. *Dynamical mechanical properties of (........) L-lysine based PUU, (------) butanediisocyanate based PUU and (——) hexanediisocyanate based PUU.*

the soft segments. Since the fusion temperature of the poly(ε-caprolactone) prepolymer is 60 °C, the higher melting temperature corresponds, at least in part to the hard block sequences. The Tg is about 14 °C higher than the Tg of pure soft segment oligomer, indicating that there is some mixing of hard segments in the soft segment phase (13,14). The DSC scan of BDI based PUU exhibits a Tg at -56.7°C and two melting endotherms at 20.2°C and 218.5 °C with respectively melting enthalpies of 22.8 J/g and 10.5 J/g. The lower Tg is an indication for better phase separation. The high melting temperature and the sharp peak are indicative of a tight packing of the hard segments. The DSC scan of HDI based PUU exhibits a Tg at -51.0 °C, a melting endotherm at 21.5 °C with a melting enthalpy of 17.3 J/g and a transition at 129 °C with a melting enthalpy of 10 J/g. Soft segments crystallinity can be compared to BDI based PUU. The higher Tg, compared to the BDI based PUU, as well as the absence of a high melting temperature are indicative of phase mixing. This is also affirmed by the fact that the melting temperature of the pure hard block is 250°C with a melting enthalpy of 66 J/g (15). The transition at higher temperature corresponds probably to the disruption of ordered segments (16,17). Between the completely amorphous and perfectly crystalline states, there exist a continuum of ordered segment morphologies.

The dynamic mechanical behavior of the polymers is shown in figure 2. All the polymers exhibit a loss modulus transition at approximately -45°C corresponding to the soft segment glass transition. The LDI based PUU shows another loss peak at 20°C which is attributed to the melting of the crystalline phase of poly(ε-caprolactone). For BDI and HDI based PUU's this transition is observed as a shoulder at 5°C (13,14). Poly(ε-caprolactone) segments in BDI and HDI based PUU's are partially crystalline to 25°C, whether in the LDI based PUU they are crystalline to 50°C. The LDI based PUU shows a small rubber plateau from 50°C to 80°C. At 90°C the hard segments of the LDI based PUU are melting, which corresponds with the DSC experiment. The BDI and HDI based PUU show a rubber plateau in the temperature range of 25°C to 150°C. For HDI based PUU this plateau is followed by a sharp drop in modulus at approximately 175°C. BDI shows a loss peak at 175°C. Thus, a small change of diisocyanate structure has a considerable effect upon the thermal behavior of the polymer. Although additionally techniques such as small angle X-ray scattering should be applied in order to draw final conclusions about the morphology, value can be set upon the data presented in this paper because they were reproducible.

Tensile properties

Tensile properties of the PUU are presented in figure 3. For comparison the tensile properties of three polyurethanes, an aromatic PU, an aliphatic PU and an aliphatic PU network, is presented in figure 4. The aromatic PU (Estane) is formed by the reaction of MDI with an adipic acid tetramethylene glycol ester, chain extended with tetramethylene glycol. The linear aliphatic PU and the aliphatic PU are formed by curing a PCL/cyclohexanediisocyanate with cyclohexanedimethanol and glycerol, respectively. The LDI, BDI and HDI based PUU's have a respective Young's modulus of 40, 52 and 38 MPa tensile strength of 17, 29 and 38 MPa, and a respective strain at break of 800, 1042 and 1168%. The stress-strain behavior of BDI based PUU is comparable to the linear aliphatic polyurethane. The higher strain at break of HDI based PUU compared to BDI based PUU is due to less ordered hard domains which can easier be deformed (18). This is also the reason for the higher tensile strength. Orientation of the polymer chains takes places under stress.

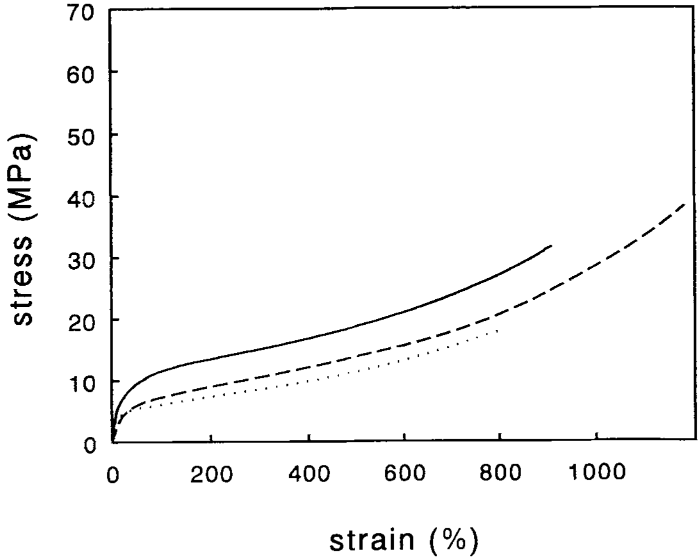

Figure 3. *Stress-strain behavior of PUU, (·········) L-lysinediisocyanate based PUU, (———) butanediisocyanate based PUU and (_ _ _ _) hexanediisocyanate based PUU.*

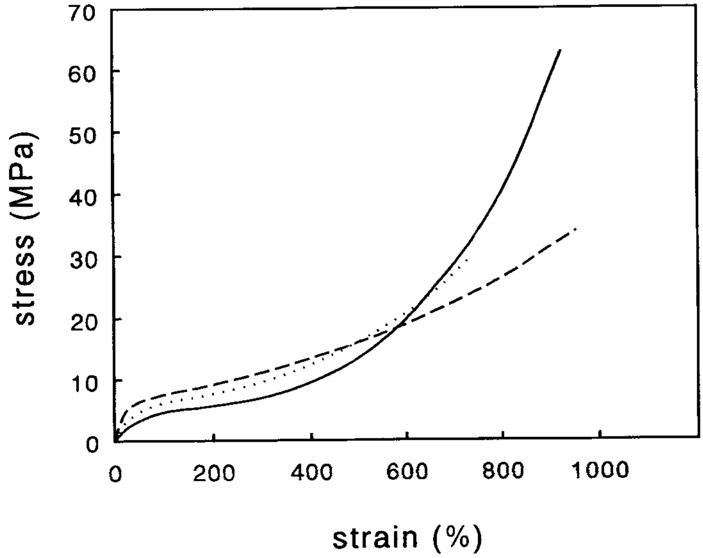

Figure 4. *Stress-strain behavior of aromatic PU (———), linear aliphatic PU (_ _ _ _) and aliphatic PU network (········).*

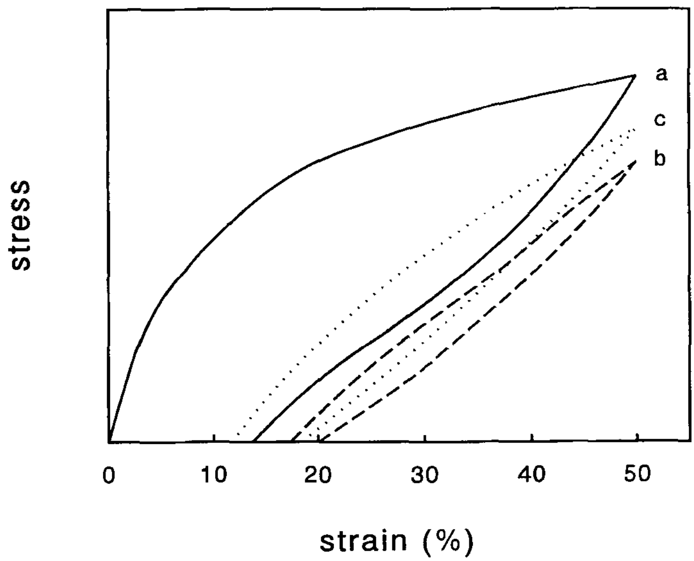

*Figure 5. Three consecutive deformation cycles up to 50% strain. **a**, first cycle; **b**, 20th cycle;c 21th cycle. Recovery time between cycle b and a is two hours.*

Table 2.

	tearing energy (kJ/m^2)	permanent deformation (%)
Aromatic PU[1]	47	10.5
Aliphatic PU, linear[2]	114	11.5
Aliphatic PU, network[3]	20.8	6.5
LDI based PUU	36	15.5
BDI based PUU	161	12.0
HDI based PUU	137	18.5

1) MDI/ adipic acid/ tetramethylene glycol based PU
2) CHDI/ cyclohexane dimethanol/ poly(ε-caprolactone) based PU
3) CHDI/ glycerol/ poly(ε-caprolactone) based PU network

Permanent set

The permanent deformation is an important parameter since it is directly related to the hysteresis phenomenon (19). Permanent deformation may shorten the time to material failure. In figure 5 the hysteresis experiment is shown. The film is deformed cyclically up to 50% initial strain. Cycle A is the first cycle, B the 20th. After a recovery time of 2 hours, cycle C was recorded. At the beginning of cycle C the permanent set is determined. The permanent sets of the PUU and PU are presented in table 2. Permanent set of BDI based PUU is 12% and can be compared to the linear aliphatic PU used for menisical reconstruction. Permanent set of HDI based PU is 18.5% due to lack of crystalline hard blocks. The permanent set of LDI based PUU is 15.5% and is an intermediate between BDI and HDI PUU's, probably due to the soft segment crystallinity. As expected, the polyurethane network shows the smallest permanent set since the hard segments, as a result of crosslinking, are not able to deform.

Tear resistance

In a previous study we concluded that, when materials are sutured in place in case of medical applications, the resistance to tear is very important to prevent the sutures from tearing out of the material (8). The tear energy can be described by (20):

$$G = 2F/h$$

where F is the applied force and h is the width of the torn path. Tear energies of PUU's and PU's are collected in table 2. The polymer network show a small resistance to tear because cracks, once formed, encounter little resistance to growth because the network chains are highly mobile (21). Eventually, strain-induced crystallization can take place. The linear PUU's and PU's show a much higher resistance to tear because two additionally processes can occur to impede crack growth. First the domains containing hard segments can be deformed and secondly their morphology can change which results in orientation. The properties depend on the degree of phase separation.

BDI and HDI based PUU shows a very high resistance to tearing compared to Estane. The tear strength of HDI based PUU is somewhat lower than for the BDI based PUU, but is still higher than for linear aliphatic PU (Elate). The crystalline hard BDI/BDA segment, which melts at 220 °C, and the phase separated morphology are responsible for the extremely high tear strength. The low tear energy of LDI based PUU is due to poor packing of the hard segments. LDI is a bulky molecule, containing an ester bond and is likely to be more compatible with ε-caprolactone segments than HDI and BDI.

Conclusions

A polyurethane urea based upon poly(ε-caprolactone), 1,4-butanediamine and butanediiso-cyanate (BDI) has been found to be semicrystalline polymer with good mechanical properties. It exhibits a relatively high tear strength due to phase separation and hard segment crystallinity. Replacing BDI by hexamethylendiisocyanate (HDI) resulted in a higher strain at break and higher tensile strength due to less ordered hard segments. It, however, increased the permanent set remarkably. Thus, a small change of diisocyanate structure has a considerable effect upon the morphology of the polymer. Replacing the diisocyanate by L-lysine diisocyante causes phase mixing. Due to the soft segment crystallinity and the lack of well ordered hard segments the polymer showed poor mechanical properties.

The fact that the BDI based PUU releases non-toxic products upon degradation, shows a relative low permanent set and shows a extremely high resistance to tear, makes this polymer very suitable for biomedical applications.

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