Reduction-sensitive rapid degradable poly(urethane-urea)s based on cystine

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ABSTRACT

Two kinds of novel reduction-sensitive rapid degradable poly(urethane-urea)s were synthesized and characterized based on a cystine derivative chain extender which provided active sites for reductive degradation. In vitro degradation study was carried out under physiological conditions mediated by glutathione and dithiothreitol respectively, and was assessed by 1H NMR, GPC and SEM. The results indicated that the disulfide bonds in poly(urethane-urea)s were effectively cleaved while the structures of urethane groups and soft segments remained almost unaffected. Still, the rate and degree of reductive degradation could be controlled by the structures of the polymers. The influence of the poly(urethane-urea)s on human umbilical vein endothelial cells was investigated by WST-1 assay. The results indicated that the polymers sustained much higher cell viability than the controls. It is possible that the poly(urethane-urea)s can be potentially applied for temporary biomaterials such as wound closure devices, cell scaffolds and sophisticated drug delivery systems.

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1. Introduction

In the past twenty years, the interest for degradable polymers have been fueled by the needs for tissue engineering, drug delivery and plastic waste problems [1–6]. As one of the premier synthetic degradable polymers, polurethanes have been extensively investigated for biomedical applications because of their inherent advantages such as biocompatibility, easily variable micro- and macro-structures, easily controllable physicochemical properties [7–9]. However, the main pathways of bonds cleavage of polyurethanes are hydrolysis, oxidative and light degradation with degradation time ranging from weeks to months and the applications for traditional polyurethanes as temporary biomaterials was limited [10–12].

It was known that reduction-sensitive cleavage is quick-response under mild conditions. The fascinating advantage induced various rapid degradable polymers containing reduction-sensitive groups in the main chain, at the side chain, or in the cross-linker [13]. Park et al. synthesized a kind of reducible poly(ethylene oxide) for drug delivery applications [14]. Lin et al. reported a series of reducible poly(amide amine)s for gene delivery [15]. Wang and coworkers developed a novel injectable hyaluronic acid hydrogels crosslinked via disulfide bond for protein delivery and cell encapsulation [16]. Hoffman et al. designed “smart” terpolymers, poly-(alkyl acrylic acid-co-butyl acrylate-co-pyridyl disulfide acrylate), which exhibited pH-dependent membrane-disruptive properties [17]. Gillies et al. reported a new polymer backbone based on N,N'-dimethylthelyenediamine and 2-mercaptoethanol linked by carbamates and thiocarbamates to proceed controlled cascade degradation [18].

Here, we proposed to employ cystine as the disulfide bond carrier, which played the role of the active sites for reduction-sensitive degradation, to develop rapid degradable poly(urethane-urea) s. It was well known that disulfide-thiol system, which is sensitive and reversible, is the major redox couple in animal tissues [19,20]. The disulfide bonds, though sufficiently stable in the extracellular environment and in vivo circulation, may be rapidly degraded under a reductive environment through disulfide-thiol exchange reactions at a time scale from minutes to hours [21]. The disulfide bonds are prone to be cleaved in cells by the action of natural tripeptide glutathione(GSH) or under abnormal reductive biological milieu of tumor tissues [22–25].

In this work, we first synthesized cystine dimethyl ester (CDE) and introduced it into the main chain of poly(urethane-urea)s...
following the simple two steps procedure (Scheme 1). Chain extension through amino groups of cystine is quick-response and under mild conditions. Cystine in vivo plays an important role in stabilizing the stereoscopic structures of peptides, proteins and activating enzymes. The molecular structure of the novel poly(urethane-urea)s combined by cystine mimicked that of protein formed by peptides and disulfide bonds connecting peptides chains. We tested the cell viability of poly(urethane-urea)s by WST-1 assay and expected the biocompatibility of the polymer may benefit from the molecular structural bionic. Still, thermal and tensile properties of poly(urethane-urea)s were studied to ensure that the poly(urethane-urea)s could be employed as potential temporary catheter and cell scaffolds.

To investigate the reduction-sensitive rapid degradation of the poly(urethane-urea)s, we employed GSH to mimic the intracellular environment. Furthermore, we selected dithiothreitol(DTT), a mild organic reducing regent commonly used to reduce DNA and protein, to mimic the abnormal reductive milieu of tumor tissues. The degradation behavior of the samples was characterized by \(^{1}\text{H} \text{NMR spectroscopy, GPC and SEM. We expected the rate and degree could be controlled by the structures of the polymers. The reduction-sensitive rapid degradation supplied a pathway different with traditional methods of polyurethanes degradation.}

2. Materials and methods

2.1. Materials

L-cystine, thionyl chloride, methanol, dibutyltin dilaurate (DBTDL), dithiothreitol(DTT) from Sino Chemical Reagent Co. Ltd.; 1,6-Hexamethylene diisocyanate (HMDI) from Bayer Co. Ltd; Glutathione from Biodee Co. Ltd. were used without further purification. Triethylamine(TEA), N,N-dimethylformamide(DMF) obtained from Sino Chemical Reagent Co. Ltd were dried before use. Polyethylene glycol (PEG, Mn:600,1000,2000) obtained from Sigma Aldrich and Polycaprolactone diol (PCL Mn:1000,2000) from Duosen Chemistry Co. Ltd were dehydrated for 3 h under 100 °C.

2.2. Measurements

NMR spectra was recorded on an Avance-400 spectrometer (Bruker, Switzerland) in DMSO at 25 °C. Chemical shifts (\(\delta\)) were reported as parts per million downfield from tetramethylsilane (TMS). Gel permeation chromatography (GPC) analyses were performed on a Perkin Elmer Series 200, using DMF as the eluent. Samples concentration was 2 mg/ml in DMF. Molecular weights were estimated against polyethylene glycol standards.

Scanning electron microscopy (SEM) micrographs were obtained on a Hitachi S-2150 field-emission scanning electron microscope. The samples were sprayed with gold particles on the surface and mounted on an aluminum stub using electric adhesive tape.

The thermal behavior of the polyurethanes was examined by DSC, using a TA Instruments Q2000. DSC data was obtained from samples of 4–6 mg at heating/cooling rates of 10 °C/min under a nitrogen flow. Thermogravimetric analyses (TGA) were performed under nitrogen atmosphere (flow rate 100 ml/min) with a TA Instruments Q5000IR from 40 to 700 °C at a heating rate of 20 °C/min.

Tensile properties were measured on the Instron 4465 Universal Electromechanical Tester equipped with a 2 kN load cell in air at 25 °C. The thickness of the samples was always close to 1 mm and the width was 4 mm. The crosshead speed was 100 mm/min with an initial length of 20 mm and samples were evaluated to determine stress and strain at break.

Poly(urethane-urea)s were recoated to films with a depth of 0.1 mm. The films were cut to 0.8 cm×0.8 cm pieces. Glutathione solution was prepared by dissolving Glutathione (0.2 M) in PBS buffer at pH 7.0 while dithiothreitol solution by dissolving dithiothreitol (0.02 M) in PBS buffer at pH 7.8. The sample films were then

![Scheme 1. Synthesis of poly(urethane-urea)s based on cystine dimethyl ester.](image-url)
Put into vials full of the degradation solution separately and shaked in a speed of 60r/min at 37°C. Samples were taken out at 1, 2, 3, 4, 8 days interval. The films immersed in PBS buffer without reductive regent at the same time intervals were employed as controls. After the degradation solution was eliminated, the films were washed with distilled water (3 × 10 mL) and put into flask with a iodoacetic acid PBS buffer solution (pH = 8.0, 0.1 M). The mixture was stirred at 25°C for 1 h to quench the degradation experiments. The liquid phase was eliminated. The films were washed with distilled water (3 × 10 mL) and then dried.

WST-1 (Beyondtime Bio-Tech, China) assay was employed to measure cell viability [28]. Poly(urethane-urea)s membranes were placed into a 24-well flat polystyrene culture plate (Corning), 500 µL Dulbecco’s Modified Eagle’s Medium (DMEM) of a human umbilical vein endothelial cell suspension (about thirty thousand cells per well) were transferred into each well and cultured for 24 h. 500 µL of fresh DMEM was used to substitute the original one before adding 1/10 (v/v) of WST-1 reagent. The cells were incubated for another 1 h, then 150 µL of the suspension in each well was transferred to a 96-well flat plate (Corning). The absorbance of the suspension was measured at 450 nm using a microplate reader. 3 specimens were tested for each sample. The cells seeded on culture plate at the same time interval were employed as controls (100% viability).

2.3. Preparation of l-cystine dihydrochloride methyl ester

l-cystine were converted to the correspondent dihydrochloride methyl esters following the similar procedure described elsewhere [26]. l-cystine, methanol and thionyl chloride were first charged in a flask and refluxed for 3 h till the mixture turned clear. The excess methanol was distilled off on a rotary evaporator. The product was recrystallized by dissolving in methanol and pouring into excess diethyl ether. The precipitate was filtered off and washed with diethyl ether. After drying under vacuum, the white powder was characterized by 1H NMR. The NMR analysis was shown in Fig. 1. 1H NMR (DMSO, ppm): 3.28 (4H, quint, CH2,a); 3.76 (6H, sing, CH3,b); 4.36 (2H, trip, CH,c); 8.71 (6H, sing, NH3+d).

2.4. Preparation of Poly(urethane-urea)s PU(PCL-HMDI-CDE)

Segmented poly(urethane-urea)s from PCL, HMDI and l-cystine dihydrochloride methyl esters were synthesized by conventional
two steps method following the similar procedure found in literature [27]. PCL and DMF was added to a three-necked flask in an oil bath at 70 °C under nitrogen. HMDI was then charged into the reactor at an NCO:OH ratio of the prepolymer equal to 2.05:1. Dibutyltin dilaurate (DBTDL) was added to the flask as a catalyst and the mixture was stirred for 3 h. After cooling down to 40 °C, L-cystine dihydrochloride methyl ester and triethylamine dissolved in DMF was slowly added to the prepolymer solution and the reaction was allowed to proceed for 16 h. The product was precipitated in distilled water and dried at 60 °C under vacuum.

Take PCL1000-HMDI-CDE for example, the 1H NMR spectrum of poly(urethane-urea)s was shown in Fig. 2.

2.5. Preparation of Poly(urethane-urea)s PU(PEG-HMDI-CDE)

Segmented poly(urethane-urea)s from PEG, HMDI and L-cystine dihydrochloride methyl esters were synthesized following the similar method of PU(PCL-HMDI-CDE). In the first step, PEG and HMDI were reacted at a 1:2.05 M ratio in DMF. Dibutyltin dilaurate (DBTDL) was added to the flask as a catalyst. The reaction was carried out at 70 °C under nitrogen for 3 h and then cooled down to 40 °C. L-cystine dihydrochloride methyl ester dissolved in DMF was slowly added to the prepolymer solution and the reaction was allowed to proceed for 18 h. The product was precipitated in anhydrous ethyl ether and dried at 60 °C under vacuum. Take PEG1000-HMDI-CDE for example, the 1H NMR spectrum of poly(urethane-urea)s was shown in Fig. 3.

3. Results and discussion

3.1. GPC and DSC analysis

The molecular weight and thermal properties of poly(urethane-urea)s were detected by gel permeation chromatography and DSC.

Table 1
The molecular weight and DSC of poly(urethane-urea)s.

<table>
<thead>
<tr>
<th>poly(urethane-urea)s</th>
<th>Diol</th>
<th>Mn</th>
<th>Mw</th>
<th>Mw/Mn</th>
<th>Tg(°C)</th>
<th>Tm(°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEG600-HMDI-CDE</td>
<td>PEG600</td>
<td>10500</td>
<td>18700</td>
<td>1.78</td>
<td>−27.4</td>
<td></td>
</tr>
<tr>
<td>PEG1000-HMDI-CDE</td>
<td>PEG1000</td>
<td>13400</td>
<td>24300</td>
<td>1.80</td>
<td>−29.2</td>
<td></td>
</tr>
<tr>
<td>PEG2000-HMDI-CDE</td>
<td>PEG2000</td>
<td>37300</td>
<td>68600</td>
<td>1.84</td>
<td>−51.8</td>
<td>30.8</td>
</tr>
<tr>
<td>PCL1000-HMDI-CDE</td>
<td>PCL1000</td>
<td>26100</td>
<td>52900</td>
<td>2.03</td>
<td>−26.6</td>
<td></td>
</tr>
<tr>
<td>PCL2000-HMDI-CDE</td>
<td>PCL2000</td>
<td>21400</td>
<td>43200</td>
<td>2.02</td>
<td>−48.2</td>
<td></td>
</tr>
</tbody>
</table>

Fig. 4. TGA curves of poly(urethane-urea)s.
and collected in Table 1. For both PEG- and PCL-poly(urethane-urea)s, their glass transition temperature (Tg) decreased with increase of soft segment molecular weight. The PEG-poly(urethane-urea)s exhibited lower Tg than the PCL-poly(urethane-urea)s with the same soft segment molecular weight. Only poly(urethane-urea) containing PEG2000 showed crystallinity with Tm 30.8 C and a melting enthalpy of 37.1 J/g. It may be attributed to the high soft segment molecular weight, which improved regularly chain packing. The poly(urethane-urea)s containing PCL showed no crystallinity because of a higher degree of phase mixing between the soft segment and hard segment. This increased phase mixing may result from disruption caused by increased compatibility between the L-cystine dimethyl ester and the PCL which all contained ester groups in chemical structures.

### 3.2. TGA analysis

In Fig. 4, all TGA curves showed a three-step degradation process. For PEG based PU, the first step degradation occurred at almost similar temperatures from 216 °C to 225 °C, which was ascribed to the thermal cleavage of chain extender [29,30]. The associated weight loss decreased from 18% to 6% with increase of soft segment molecular weight. The second step at temperatures from 329 °C to 341 °C may assign to the thermal cleavage of hard segments in PU. The associated weight loss decreased from 38% to 11% agreed with the theoretical data relatively. The third step temperature of PEG600PU was much higher than that of PEG1000PU or PEG2000PU because of the lowest PEG molecular weight.

<table>
<thead>
<tr>
<th>Poly(urethane-urea)s</th>
<th>Tensile strength (MPa)</th>
<th>Strain (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEG600-HMDI-CDE</td>
<td>5.6</td>
<td>537.5</td>
</tr>
<tr>
<td>PEG1000-HMDI-CDE</td>
<td>4.0</td>
<td>711.4</td>
</tr>
<tr>
<td>PEG2000-HMDI-CDE</td>
<td>3.0</td>
<td>833.2</td>
</tr>
<tr>
<td>PCL1000-HMDI-CDE</td>
<td>12.0</td>
<td>438.3</td>
</tr>
<tr>
<td>PCL2000-HMDI-CDE</td>
<td>10.4</td>
<td>513.3</td>
</tr>
</tbody>
</table>

Table 2: Tensile properties of poly(urethane-urea)s.

Fig. 5. 1H NMR spectroscopy of PEG1000PU after 0, 2 and 4 days of degradation mediated by glutathione.

Fig. 6. 1H NMR spectroscopy of PCL1000PU after 0, 2 and 4 days of degradation mediated by glutathione.
In contrast, the first step degradation process of PCL based PU occurred at relative 231 °C higher than those of PEG based PU. It may ascribe to the different phase state formed by PCL based PU. The associated weight loss decreased from 12% to 9% with increase of soft segment molecular weight. The second step occurred at still similar temperatures from 337 °C to 343 °C. The third step temperature of PCL1000PU was much higher than that of PCL2000PU, depending on the lower PCL molecular weight.

### 3.3. Stress-strain test

Stress-strain test results were given in Table 2. The data indicated that the broken tensile strength of both kinds of poly(urethane-urea)s decreased with increase of soft segment molecular weight. Considering the total polymer molecular weight of PEG600 PU was almost the same with the PEG1000 sample, increase of PEG molecular weight and soft segment content leaded to weaker tensile properties. Although the total polymer molecular weight of PEG2000PU was much higher, previous researches have indicated that increasing total polymer molecular weight above 25,000 has little effect on physical properties of polyurethane [31]. Thus, the increase of polymer molecular weight of PEG2000 PU was not believed to change the trend noted in the tensile properties. Broken strain of both PEG and PCL based PU increased with increase of soft segment molecular weight. They may result from higher soft segment molecular weight and soft segment content.

### 3.4. Degradation behavior mediated by glutathione

The degradation behavior of the poly(urethane-urea)s mediated by glutathione was examined to follow the intensity of the hydrogen atoms in methylene groups next to the disulfide bond (δ = 3.0ppm) by $^1$H NMR Spectroscopy. Figs. 5 and 6 showed the $^1$H NMR Spectroscopy of PEG1000PU and PCL1000PU after 0, 2 and 4 days of degradation mediated by glutathione respectively. The decreased intensity of the hydrogen atoms (δ = 3.0ppm) for both PU corresponded to cleavage of disulfide linkages. Specifically for PEG based PU, peak area decreased about 15% after 2 days degradation and around 25% after 4 days, while about 10% after 2 days degradation and about 20% after 4 days degradation for PCL based PU. It indicated that the disulfide bonds in polyurethanes were cleaved by glutathione. Moreover, the appearance of the peak (δ = 3.9ppm) in Fig. 5 related to the hydrogen atoms in methylene groups between the sulphur atoms and carboxyl indicating that the free thiol group generated upon degradation was entrapped to

![Fig. 7. Degradation of the poly(urethane-urea)s mediated by glutathione.](image)

![Fig. 8. SEM micrographs of the poly(urethane-urea)s before and after 8 days of degradation mediated by glutathione. PEG2000PU before degradation (a), PEG2000PU after degradation (b), PCL1000PU before degradation (c), PCL1000PU after degradation (d).](image)
thioether. The same peak for PCL based PU was covered by the huge peak in the region between 3.9 and 4.0 ppm. The peaks appeared at 7.1 ppm, 6.3 ppm and near 1 ppm related to the hydrogen atoms in urethane groups, urea groups and methylene of soft segments respectively. They all kept almost constant before and after degradation revealing that the collapse of the polymer structure mainly resulted from the cleavage of disulfide linkages rather than bonds of soft segments, urethane and urea groups.

Fig. 9. $^1$H NMR spectroscopy of PEG1000PU after 0, 2 and 4 days of degradation mediated by dithiothreitol.

Fig. 10. $^1$H NMR spectroscopy of PCL1000PU after 0, 2 and 4 days of degradation mediated by dithiothreitol.
PCL based PU may lead to different degradation rates on the surface of more hydrophobic PCL2000. The hydrophobicity of PCL1000 was fastest, while that of PCL2000PU was slowest because of the rich in the outer layers. The number-average molecular weight of control samples decreased slightly about 7%. The degradation rate of PEG2000PU was the fastest, while that of PEG1000PU was slowest because of the rich hydrophobic PCL2000. The hydrophobicity of PCL2000 was highest, while that of PCL1000 was lowest because of the rich hydrophilic PEG2000. The number-average molecular weight of control samples decreased slightly about 10%. Since dithiothreitol was small enough, as a result, glutathione and dithiothreitol can not cleave disulfide bonds of poly(urethane-urea)s. The reduced glutathione exchanged to the oxidation state after the reaction. The thiol-disulfide exchange reaction [16]. In the case, the possible mechanism of degradation of poly(urethane-urea)s mediated by glutathione was shown in Scheme 2. The thiol groups of glutathione first interacted with the disulfide bonds of poly(urethane-urea)s to form a transition state. The transition state was not stable and prone to rapid cleavage. The disulfide bonds of poly(urethane-urea)s form free thiol groups while the reduced glutathione exchanged to the oxidation state after the reaction.

3.5. Degradation behavior mediated by dithiothreitol

The degradation of the poly(urethane-urea)s mediated by dithiothreitol was also assessed by the changes in the structure of the polymer. Figs. 9 and 10 showed the $^1$H NMR Spectroscopy of PEG1000PU and PCL1000PU after 0, 2 and 4 days of degradation mediated by dithiothreitol respectively. Similarly, the decreased intensity of the hydrogen atoms in methylene groups next to the disulfide bonds ($\delta = 3.0$ppm) indicated that disulfide bonds were prone to be attacked by dithiothreitol. Peak area related to hydrogen atoms in methylene groups next to the disulfide bonds ($\delta = 3.0$ppm) decreased about 20% after 2 days incubation and around 35% after 4 days, while 30% after 2 days degradation and about 50% after 4 days for PCL based PU. The almost constant area of the peaks appeared at 7.1ppm, 6.3ppm and near 1ppm also demonstrated the cleavage of disulfide linkages by the action of dithiothreitol. It also revealed that bonds of soft segments, urethane and urea groups were almost not affected during degradation.

The number-average molecular weight loss of poly(urethane-urea)s exposed to dithiothreitol solution presented that the poly(urethane-urea)s decreased obviously from the first day to the forth day, finally to a constant level of about 45% loss. (Fig. 11). In contrast, the number-average molecular weight of control samples decreased slightly about 10%. Since dithiothreitol was small molecular and well water soluble, it may disperse deeply and fast into the inner parts of films. Sample films were still not thin enough. As a result, glutathione and dithiothreitol can not cleave the disulfide bonds embedded deeply.

The degradation of poly(urethane-urea)s mediated by dithiothreitol followed similar mechanism as the degradation mediated by glutathione. The main distinction was the dithiothreitol finally formed stable cyclic dithiol structure by itself after the disulfide bonds of poly(urethane-urea)s were cleaved into thiol groups.

The SEM analysis of poly(urethane-urea)s before and after degradation showed that holes were dense and obvious on the surface of PCL2000PU for 4 days in 0.02 M dithiothreitol solution at pH 7.8. The SEM micrographs of the PCL2000PU before 4 days of degradation mediated by dithiothreitol (a), after degradation (b).
thermal stability to act as potential biomaterials. Still, thermal and physical characterization revealed that the novel based on PCL showed a great biocompatibility on endothelial cells. Degradation of all polymers especially the PCL based resulted in faster degradation. In contrast, more strong the counterparts with PCL, and the higher diol monomers molec- degradation was mediated by glutathione, the rate of dation behaviors for the poly(urethane-urea)s. Generally, when the was recorded by GPC. It was found that alteration of the soft characterized by 1H NMR and the number-average molecular weight resulted in faster degradation. In contrast, more strong degradation was mediated by glutathione, the rate of poly(urethane-urea)s derivatives degradable in reductive conditions. Biomacromolecules 2005;6:24–6. the poly(urethane-urea)s. Novel bioreducible poly(amide amine)s for highly efficient gene delivery. Bioconjugate Chemistry 2007;18:138–45. a physiological environment. The changes in structure were char- acterized by 1H NMR and the number-average molecular weight was recorded by GPC. It was found that alteration of the soft segment types and molecular weight resulted in variable degra- dation behaviors for the poly(urethane-urea)s. Generally, when the degradation was mediated by glutathione, the rate of poly(urethane-urea)s with PEG as soft segments was higher than the counterparts with PCL, and the higher diol monomers molec-ular weight resulted in faster degradation. In contrast, more strong reducing property of diithioctreitol led to more thorough degradation of all polymers especially the PCL based poly(urethane-urea)s in view of the lower concentration of diithioctreitol. The results of cells viability test indicated the PU based on PCL showed a great biocompatibility on endothelial cells. Still, thermal and physical characterization revealed that the novel poly(urethane-urea)s have the certain mechanical property and thermal stability to act as potential biomaterials.

3.6. Cell Viability

Cell viability of the PCL based PU was established in human umbilical vein endothelial cells using the WST-1 assay (Fig. 13). After incubating for 24 h, endothelial cells cultured on PCL1000PU accelerated to proliferate greatly with the viability of 704.1% compared to the control as 100% and the viability of PCL2000PU reached 544.8% also at a high level. It indicated that PCL based PU demonstrated seldom negative effects on short time cells culturing. The distinct of viability between PCL1000PU and PCL2000PU might be due to different hydrophilcity and surface morphology.

4. Conclusion

Two series of novel reduction-sensitive rapid degradable poly(urethane-urea)s have been successfully synthesized. Cystine dimethyl ester as the chain extender provided active sites for reductive degradation. The linear polymers were degraded by the action of tripeptide glutathione and diithioctreitol respectively to investigate the performance of the poly(urethane-urea)s in a physiological environment. The changes in structure were char-acterized by 1H NMR and the number-average molecular weight was recorded by GPC. It was found that alteration of the soft segment types and molecular weight resulted in variable degra- dation behaviors for the poly(urethane-urea)s. Generally, when the degradation was mediated by glutathione, the rate of poly(urethane-urea)s with PEG as soft segments was higher than the counterparts with PCL, and the higher diol monomers molec-ular weight resulted in faster degradation. In contrast, more strong reducing property of diithioctreitol led to more thorough degradation of all polymers especially the PCL based poly(urethane-urea)s in view of the lower concentration of diithioctreitol. The results of cells viability test indicated the PU based on PCL showed a great biocompatibility on endothelial cells. Still, thermal and physical characterization revealed that the novel poly(urethane-urea)s have the certain mechanical property and thermal stability to act as potential biomaterials.