Statement of Purpose

Poly (amino acids) are a natural choice for different biomaterial applications, including tissue engineering, because amino acids are metabolites. However due to difficulties related to synthesis, purification, and processing, poly (amino acids) are very restricted in application. To avoid these problems, pseudo-poly (amino acids) are exploited as an alternative, where the amide linkages of the peptides are replaced by non-amide linkages.

L-tyrosine based pseudo-poly (amino acids) are widely investigated[1,2]. Several non-amide linkages are utilized to synthesize L-tyrosine based pseudo-poly (amino acids), but further development is warrented. In this work we report the synthesis and characterization of L-tyrosine based polyurethanes for tissue engineering applications. This class of pseudo poly (amino acids) offers a better chance to control the structure and the properties of the material. Polyurethanes have the general structure of P-$(D(CD)_n\text{-}P)_m$, where, P is polyol, D is diisocyanate, and C is chain extender. The portion of the polyurethane comprising C and D represent the hard segment and P represents the soft segment of the polymer. L-tyrosine based dipeptide monomer (DTH) is incorporated as a chain extender molecule with polyethylene glycol (PEG) and polycaprolactone diol (PCL) as the polyol and hexamethylene diisocyanate (HDI) and dicyclohexylmethane-4,4'-diisocyanate (CHMDI) as the diisocyanate. By using different combinations and compositions of the components, a class of L-tyrosine based polyurethanes were synthesized and characterized for tissue engineering applications.

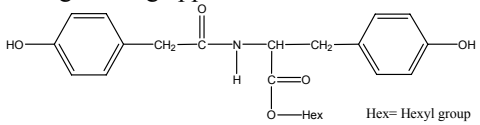

Figure 1. Structure of DTH

Materials, Method and Analytical Procedures

►**Materials.** DTH was synthesized according to literature from L-tyrosine and desaminotyrosine[1]. PEG (M_w 1000), PCL (M_w 1250), HDI, CHMDI, Stannous Octoate ($Sn(Oct)_2$), Dimethyl formamide (99%), Chloroform (99%), Sodium chloride (NaCl) were used. All the solvents and materials were dried before use. Deionized water was used for all purposes.

►**Method.** The polyurethanes were synthesized by standard two step method under inert N_2 atmosphere. In the first step, the polyol is reacted with diisocyanate in DMF (solvent) in 1:2 molar ratios at 110°C for 3 hours with $Sn(Oct)_2$ as catalyst. After this step, the reaction was cooled down to room temperature and the DTH was as the proportion of the polyol and the temperature was raised to 80°C. After 12 hours, the reaction was quenched in cold saturated NaCl solution. The polymer precipitated out was either filtered or centrifuged depending on the physical characteristics of the polymer.

►**Characterization and Analytical Procedures.** The polymerization reactions and the structure of the polymers were studied by FTIR. Thermal behaviors were assessed by DSC and TGA. Biodegradation of the polymers was studied by measuring mass loss over time stored in PBS solution (37°C, pH~7.4). Surface characteristics were assessed by water contact angle.

Results

Four different L-tyrosine based polyurethanes were synthesized by altering the two polyols and the diisocyanates. The nomenclature used for the synthesized polyurethanes are as: P-D-C, where P is either PEG or PCL, D is either HDI or CHMDI, and C is DTH. The typical FTIR spectra obtained to study the progress of the reactions is shown in Figure 2, which shows the appearance of isocyanate and urethane groups in the prepolymer and the disappearance of isocyanate and existence urethane groups in the polymer indicating successful polymerization.

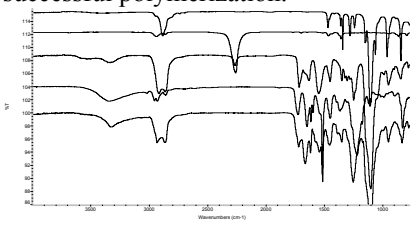

Figure 2. FTIR

Table 1 shows DSC results of two T_g's corresponding to hard and soft segments of the polymer and the same range of decomposition temperature (T_d). Table 1 also summarizes the weight remaining for the polymers after 30 days of degradation and the contact angle values.

Property/ Polymers	PEG-HDI-DTH	PCL-HDI-DTH	PEG-CHMDI-DTH	PCL-CHMDI-DTH
T_g (soft segment)	-40°C	-44°C	-42°C	-42°C
T_g (hard segment)	0°C	2.5°C	2.5°C	4.5°C
T_d	305°C	316°C	311°C	321°C
% Weight Remaining	72	90	73	85
Contact Angle(°)	33	75	56	80

Table1. Summary of results

These results shows that L-tyrosine based polyurethanes can be successfully synthesized with a range of processing temperatures. The substantial biodegradation behavior of the polymers is useful for tissue engineering applications. Relative surface hydrophobicity and hydrophilicity are also important.

Conclusion

The results indicate that the properties of L-tyrosine based polyurethanes can be easily tuned over a wide range, which makes these materials promising for tissue engineering applications. Moreover other options to change the properties that are under investigation include the blend of polyurethanes, use of different chain extenders and copolymerization.

References

1. Gupta, A. S.; Lopina, S. T; *Polymer* 2004, 45(14), 4653
2. Bourke, S. L.; Kohn, J., *Advanced Drug Delivery Reviews* 2003, 55(4), 44