From Biostable to Biodegradable Polymers for Biomedical Applications

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INTRODUCTION

Biostable polymers including nylon, polyethylene terephthalate (PET), poly (1, 4-butylene terephthalate) (PBT) and polyurethanes are used extensively for making fibers and molding articles[1]. Some of these are used in a variety of biomedical applications such as non-absorbable surgical sutures, tissue engineering scaffolds, films, foams, short-term medical devices (catheters, endotracheal tubes, cannulas), long-term implantable devices (vascular prostheses, intra-aortic balloons), tissue engineering scaffolds, infusion pumps and cardiac pacemakers etc and are considered to be safe and biocompatible. Unfortunately, these polymers are non-absorbable and, therefore, cannot be used in those medical applications where biodegradability is a desired feature such as biodegradable sutures or as biodegradable polymers for controlled release of biologically active agents.

The widespread availability and applications of these biostable polymers makes it imperative to enhance their native value, for example, by transforming them into biodegradable polymers through chemistry. The resulting polymers will have physical properties of biostable polymers and controlled degradation profile of an absorbable polymer. These polymers with combined attributes of biostable and biodegradable polymers will enable us to meet the unmet requirements in medical device industry and biomedical applications where biodegradable polymers with physical properties of biostable polymers are needed.

Motivations to incorporate biodegradability into the backbone chain of a biostable polymer led us towards the development of biodegradable nylon, poly(ethyleneterephthalate) and polyurethanes. These biodegradable polymers were prepared from their precursor monomers wherein these precursor monomers were functionalized with safe and biocompatible molecules including L-lactide, glycolide, p-dioxanone and caprolactone, prior to polymerization. These monomers are the building blocks of majority of biodegradable polymers used to make commercial medical devices such as sutures, staples, orthopedic screws and implantable surgical devices to tissue engineering scaffolds.

Key aspects of these novel polymers having combined attributes of biostable and biodegradable polymers will be discussed. Synthesis and characterization of these polymers will be presented. Preliminary results from invitro hydrolytic degradation studies will also be presented. We believe that innovative technology behind these polymers will enable us to make absorbable medical devices that can fulfill the unmet needs of the healthcare community.

RESULTS AND DISCUSSION

Biodegradable Nylon. Biodegradable Nylon with varying hydrolytic degradation profiles were prepared from adipic acid and hexamethylenediamine monomers functionalized with varying safe and biocompatible molecules including glycolic acid, lactic acid, open chain form of caprolactone and p-dioxanone. As shown in figure 1, biodegradable nylon was prepared from hexamethylene diamine and adipic acid functionalized with safe and biocompatible glycolic acid molecule. Similarly, as shown in figure 2, biodegradable nylon was prepared from glycolic acid functionalized adipic acid and glycolic acid functionalized hexamethylenediamine.

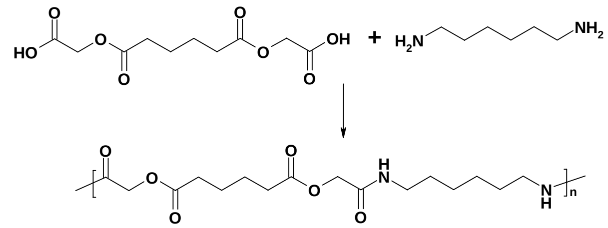

Figure 1. Biodegradable Nylon prepared from glycolic acid functionalized adipic acid and hexamethylenediamine.

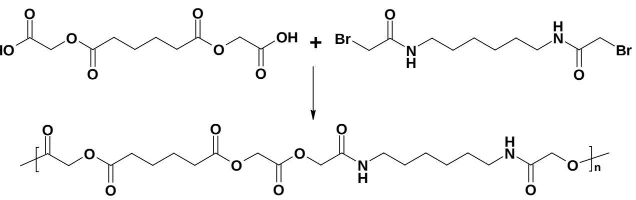

Figure 2. Biodegradable Nylon prepared from glycolic acid functionalized adipic acid and functionalized hexamethylenediamine

Nylons and other polyamides from novel end functionalized diacids and hexamethylenediamine monomers will not only be biodegradable but will also possess toughness and mechanical properties of that of commercially available nylon. These biodegradable nylons and polyamides will degrade into safe and biocompatible degradation products upon hydrolysis. These biodegradable nylons and other polyamides may find applications in sutures, films, medical device packaging, coatings, adhesion prevention barriers and tissue engineering.

Biodegradable Poly(ethyleneterephthalate): Biodegradable PET was prepared from glycolide and lactide functionalized terephthalic acid monomer and diol such as ethylene glycol via condensation polymerization. The resulting PET polymer is expected to have controlled hydrolytic degradation profile. In addition to glycolide and lactide, terephthalic acid was also functionalized with open chain of caprolactone, and open chain of p-dioxanone. The polymers derived from these functionalized terephthalic acid resulted in different hydrolytic degradation profiles. Furthermore, the PET polymers derived form functionalized terphthalic acid are expected to be sterilizable by gamma radiation while still retaining a desirable level of physical and biological properties unlike the commercially available synthetic absorbable polymers used to prepare implantable surgical devices.

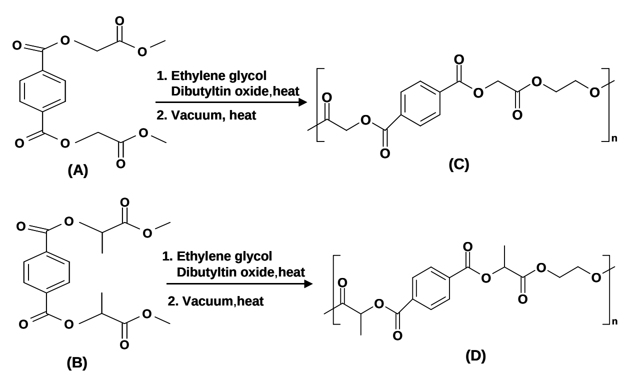

Figure 2. (A) Methyl glycolate functionalized terephthalic acid (B) Methyl lactate functionalized terephthalic acid (C) & (D) Biodegradable PET polymers.

These polymers are attractive candidates for a large number of potential biomedical applications such as implantable surgical devices, controlled release of drugs, films, adhesion prevention barriers and radiation stable sutures.

Biodegradable Polyurethanes. Biodegradable polyurethanes were prepared from highly reactive isocyanates that are similar to MDI but are biodegradable and have tunable hydrolytic degradation profiles. What distinguishes our isocyanates from the commonly used isocyanate, MDI, is the presence of a degradable linkage bridging the aromatic rings in figure 3(b) instead of the non-degradable methylene group as shown in figure 3 (a). Furthermore, the degradable linkage in our isocyanates is derived from safe and biocompatible glycolic acid, lactic acid, caprolactone, p-dioxanone and diols such as ethylene glycol. These monomers are the key components of majority of biodegradable polymers used to make commercial medical devices.

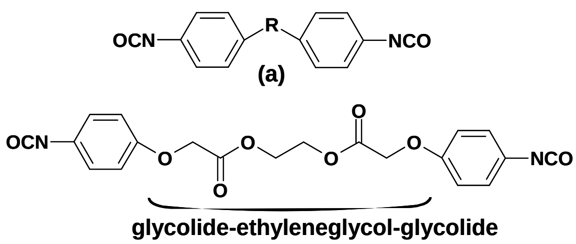

Figure 3. (a) MDI, Methylene diphenyl isocyanate, R is a CH_2 group (b) Biodegradable aromatic diisocyanate similar to MDI derived from safe and bicompatible glycolic acid and ethylene glycol monomers.

Polyurethanes derived from these novel isocyanates and chain extender diols are expected not only be biodegradable but also possess for the first time degradable hard segments. Furthermore, the hydrolytic degradation rate of these polyurethanes can be controlled by (a) deriving the degradable hard segment from different safe and biocompatible molecules and (b) varying the chain length of the repeat units derived from absorbable, safe and biocompatible glycolic acid, lactic acid, p-dioxanone and caprolactone monomers in the linker bridging the aromatic rings in the hard segment. Moreover, these polyurethanes will have toughness and mechanical properties of that of commercially available medical grade polyurethanes and biodegradability of commercial biodegradable polymers. In addition, the derived biodegradable polyurethanes will degrade into safe and biocompatible degradation products unlike polyurethanes derived from MDI.

CONCLUSIONS

We have developed biodegradable nylon, PET and polyurethanes that have combined attributes of a biostable and a biodegradable polymer. These polymers are expected to find use in a variety of biomedical applications including controlled drug delivery, wound care applications, adhesion prevention, tissue adhesives and sealants, medical devices, medical device coatings and tissue engineering.

REFERENCES

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