Novel Absorbable Polymers from Functionalized Diglycolic Acid

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Introduction:

A number of commercially available absorbable medical devices and surgical products are based upon homopolymers or copolymers formed by ring opening polymerization of five key monomers i.e. glycolide, lactide, caprolactone, p-dioxanone and trimethylene-carbonate. Among them homopolymer of glycolide i.e. polyglycolide or polyglycolic acid and copolymers containing glycolic acid repeat units are of great interest for biomedical applications. For example, polyglycolide (Dexon^{TM}), poly(lactide-co-glycolide) (Vicryl^{TM}) and poly(caprolactone-co-glycolide) (Monocryl^{TM}) have found use as a suture or mesh material. The key to the biomedical success of these polymers lies in their ability to get hydrolyzed into their α-hydroxy acid constituent such as lactic acid, glycolic acid and hydroxyhexanoic acid. These constituents are eliminated by the usual physiological metabolic pathways and hence make these polymers safe and biocompatible.

Since repeat units derived from glycolic acid is the common feature and the key component of majority of commercially available absorbable polymers, the objective of the current work is to develop novel functionalized diglycolic acid monomers wherein the diglycolic acid has been conjugated with either glycolic acid, lactic acid, caprolactone and combinations thereof. The resulting monomers were then polymerized by condensation with diols to yield absorbable polyesters that incorporates attributes of diglycolic acid.

Results and Discussion:

Functionalization of Diglycolic acid: Diglycolic acid molecule (*Figure 1a*) was symmetrically conjugated with glycolic acid, lactic acid and a combination of glycolic acid and caprolactone via esterification as shown in figure 1b, 1c and 1d respectively to yield functionalized diglycolic acid monomers with varying hydrolytic degradation profiles. These monomers were then subjected to condensation polymerization with ethylene glycol to yield novel absorbable aliphatic polyesters as shown in figure 2 (a)-(c). The monomers as well as the polymers in the present study will have different hydrolytic degradation rate. Glycolic acid functionalized diglycolic acid and corresponding polymers will hydrolyze faster than lactic acid and Caprolactone functionalized diglycolic acid and corresponding absorbable polymers. Furthermore, the hydrolytic degradation rate can also be controlled by using different combinations of functionalization moieties to prepare functionalized diglycolic acid monomers.

Moreover, the hydrolytic degradation rates of the aliphatic polyesters derived from functionalized diglycolic acid monomers can be controlled by varying the chain length as well as the nature of the diol during polymerization. For example, using polyethylene glycol instead of ethylene glycol will result in more hydrophilic aliphatic polyester. Similarly, using diol of different chain lengths can yield polyesters, which are solid at room temperature to those, which are liquid at room temperature. In addition, these functionalized diglycolic acid monomers can also be condensed with biologically active as well as non-active diamines to yield polyesteramides.

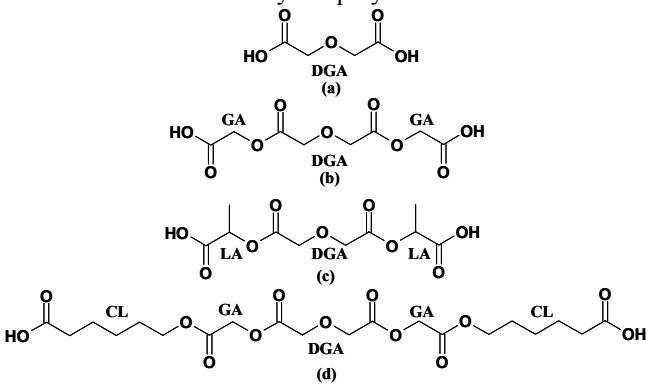

Figure 1. Novel functionalized diglycolic acid monomers where GA is glycolic acid, LA is Lactic acid, CL symbolizes caprolactone unit, DGA symbolizes diglycolic acid and EG stands for ethylene glycol unit.

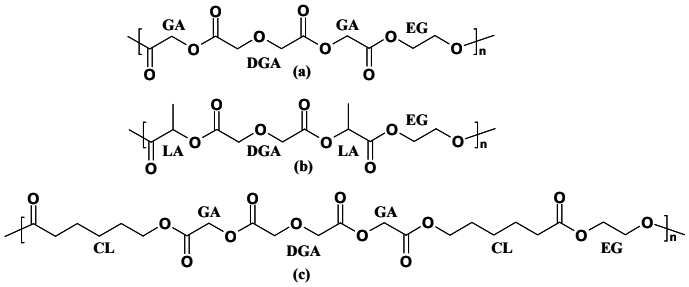

Figure 2. Absorbable polymers derived from (a) GA functionalized diglycolic acid (b) LA functionalized diglycolic acid and (c) GA and CL functionalized diglycolic acid monomers

Aliphatic polyesters with different hydrolytic degradation rates derived from these functionalized diglycolic acid monomers will find applications for controlled release of injectable drugs, medical device coatings, cosmetics and adhesion prevention barriers. The synthesis and characterization of functionalized diglycolic acid monomers as well as the corresponding polymers will be presented in the meeting.

References:

(1) Bezwada, R, S., US Patent Application No.12/212,293