

Absorbable polymers from functionalized Tyrosine

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Introduction:

The past 20 years have seen increased interest in synthetic absorbable polymers derived from natural amino acids for various biomedical applications. Such interest has been driven by virtue of these polymers being analogs of natural tissue and degradable under physiological conditions into constituent amino acids. Besides building cells and repairing tissue, amino acid derived polymers (proteins) form antibodies to combat invading bacteria & viruses; they are part of the enzyme & hormonal system; they build nucleoproteins (RNA & DNA); they carry oxygen throughout the body and participate in muscle activity. Out of the 22 known naturally occurring amino acids, eight are essential (cannot be manufactured by the body) the rest are non-essential (can be manufactured by the body with proper nutrition).

Tyrosine is one of the non-essential amino acid. It is a parent amino acid for skin, hair and eye pigments. Furthermore, it is an important precursor for neurotransmitters epinephrine, nor epinephrine and dopamine and hence plays an important role in transmission of nerve impulses to the brain; helps overcome depression; improves memory; increases mental alertness; and promotes the healthy functioning of the thyroid, adrenal, and pituitary glands. Such attractive properties of tyrosine led many research groups to develop absorbable polymers from tyrosine. However, tyrosine derived polymers developed and studied so far have either very slow or incomplete biodegradation or have marginal engineering properties. These have been the major obstacles for the practical applications of these polymers for biomedical applications. This necessitates the need to develop novel biocompatible and absorbable tyrosine based polymers with combined attributes of excellent engineering properties, improved efficacy and tunable hydrolysis profile.

This paper describes the synthesis of functionalized tyrosine and absorbable polymers derived from it that are useful for drug delivery, tissue engineering, stent coatings, stents, and implantable medical devices. Tyrosine is functionalized with safe and biocompatible molecules (e.g. glycolic acid, lactic acid, caprolactone, and dioxanone). Synthesis and characterization of functionalized tyrosine monomers and polymers will be presented. *In Vitro* hydrolysis and the controllable hydrolysis profiles will be discussed during presentation.

Results and Discussion:

Functionalization of Tyrosine: Tyrosine molecule contains a hydroxyl, carboxylic acid and an amine group. In the present study, either of these functional groups in tyrosine were functionalized with glycolic acid, lactic acid and caprolactone moiety as shown in figure 1. This

functionalization resulted in the formation of novel absorbable tyrosine monomers which were then either self condensed or condensed with ethylene glycol to yield novel absorbable polymers containing tyrosine in the polymer backbone as shown in figure 2. All functionalized tyrosine monomers and polymers derived from them were characterized using NMR spectroscopy. The details of the monomer and polymer synthesis and their characterization will be presented in the meeting.

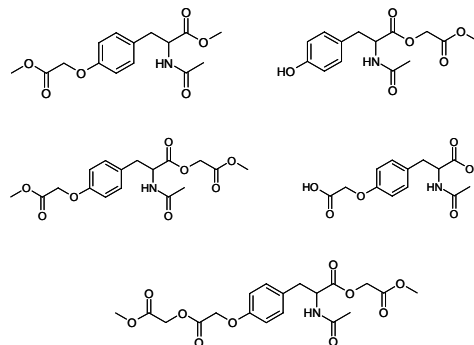


Figure 1. Functionalized Tyrosine Monomers

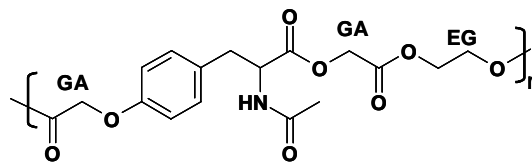


Figure 2. Absorbable Polymer from functionalized Tyrosine monomer, GA-Glycolic acid, EG-Ethylene glycol

Conclusions: For the first time, absorbable polymers have been developed from functionalized tyrosine monomers. These polymers not only have a controlled hydrolytic degradation profiles but are also anticipated to degrade into safe and biocompatible molecules. These polymers are excellent candidates for drug delivery, stent coatings, sutures and tissue engineering.

References:

- (1) (a) Kohn et al. U.S. Patent. 5,099,060 (b) Bezwada Rao S. PMSE Preprints, 2006, 95,399 (c) Bezwada Rao S. PMSE Preprints, 2006, 95,825 (d) Bezwada Rao S. US Patent Application No. 60/726341.