Absorbable Polymers from Functionalized Amino Acids

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INTRODUCTION

This paper describes the synthesis of functionalized of amino acids, especially phenol containing amino acids, and absorbable polymers derived there from, that are useful for drug delivery, tissue engineering, stent coatings, stents, and implantable medical devices.

Amino acids are the "building blocks" of the body. Besides building cells and repairing tissue, they 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. When a protein is broken down by digestion the result is 22 known 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. Tyrosine transmits 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.

Absorbable polymers[1] of diphenolic monomers based on 3-(4-hydroxyphenyl) propionic acid and L-tyrosine alkyl esters (desaminotyrosyl-tyrosine alkyl esters) were reported. The rate of biodegradation is slow for the polymers made from these monomers. Poly (glycolic acid) (PGA), poly (lactic acid) (PLA) and their copolymers are widely used synthetic, degradable polymers due to their established record of safety and FDA approval. Poly (amino acids) derived from naturally occurring alpha.-L-amino acids are another major group of degradable polymers. Despite their apparent potential as biomaterials, poly (amino acids) has actually found few practical applications. A major problem is that most of the poly (amino acids) is highly non-processible, which limits their utility. Although several copolymers of hydroxyl acids and amino acids have been prepared and evaluated from a biological perspective, their investigation as biomaterials has been rather limited [2].

The object of our work is to prepare a novel functionalized amino acids and absorbable polymers derived from them. The amino acids are functionalized with safe and biocompatible molecules (e.g., glycolic acid, lactic acid, caprolactone, and dioxanone). The polymers derived from the novel functionalized amino acids are expected to have controllable hydrolysis profiles, improved bioavailability, improved efficacy, and enhanced functionality. Some of the functionalized amino acids can be monomers from which polymers can be made that are useful for medical applications. For example, phenol containing amino acids (e.g., L-tyrosine) can be functionalized to form functionalized monomers that can then be polymerized to form absorbable polymers (e.g., polyesters, polyamides, polyester amides, polyurethanes, and polyanhydrides.

Synthesis and characterization of these monomers and polymers will be presented. *In Vitro* hydrolysis and the controllable hydrolysis profiles will be discussed.

REFERENCES

1. Kohn et al. U.S. Pat. 5,099,060.
2. (a) Helder et al., J. Biomed. Mater. Res., (24), 1005-1020 (1990) discloses the synthesis of glycine and DL-lactic acid copolymers and the resulting in vitro and in vivo degradation. (b) Barrera et al., Macromolecules, (28), 425-432 (1995). (c) U.S. Pat. 3,773,737.

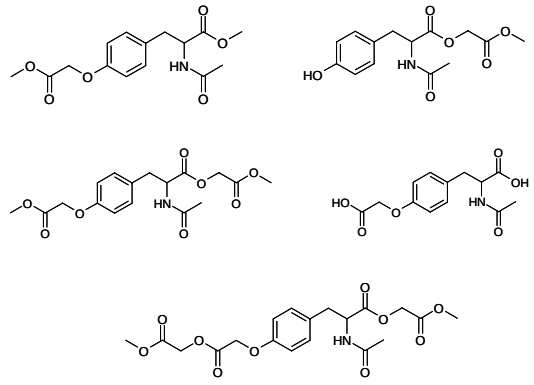

Figure 1. Novel functionalized amino acids.