Synthesis and Characterization of Novel Absorbable Polymers from Functionalized Phenolic monomers

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INTRODUCTION

Commercially available bioabsorbable and biocompatible polymers such as polylactide (PLA), polyglycolide (PGA) and polycaprolactone are of great interest for biomedical applications. These polymers are synthesized by ring opening polymerization of lactone monomers such as lactide, glycolide and ε-caprolactone respectively. These polymers have the advantage of being readily hydrolyzed into their α-hydroxy acid constituent such as lactic acid, glycolic acid and hydroxyhexanoic acid, which are eliminated by the usual metabolic pathways and hence considered to be safe and biocompatible polymers.

The impetus of research over the past few years is directed towards development of novel or modified biomaterials with improved biodegradation characterstics and mechanical properties. Of great interest are polylactones with phenolic moieties. Phenolic compounds or phenolics in the context of the present work are defined chemically as substances which have one or more aromatic rings and bears one or more hydroxyl substituents on the ring. Phenolic and phenolic compounds are found widely in nature: seeds, plant oils, vegetables, tea, coffe beer, wine, herbal products. Many Phenloic compounds exhibit antioxidative, antiinflammatary, antimutagenic, and anticarcinogenic properties. Phenolics have many valuable uses in the field of nutrition, nutriceuticals, pharmaceuticals, agricultural chemistry. Some of the examples of which include the residue of phenols, naphthols, flavonoids, isoflavonoids, coumarins, chromones, chalcones, cinnamic acids, simple benzoic acids, indoles, acetophenones, benzophenones, alkaloids, catechins, catechols, hydrocinnamic acids, phenolic acids, resorcinol, hydroquinone, drugs containing phenolic groups, natural products containing phenolic groups, amino acids containing phenolic groups, and drugs containing naphthols; Some of the examples of natural phenolics are caffeic acid, capsaicin, daidzein, ferulic acid, isopimpinellin, resveratrol, synapic acid, vanillic acid, and vanillin. Therefore, most of the phenolics are considered to be safe and biocompatible.

This paper describes the synthesis of novel functionalized phenolic monomers as shown in figure 1 from phenollics and hydroxy acids such as Glycolic acid, lactic acid, open chain caprolactone, open chain p-dioxanone and their subsequent polymerization to form functionalized degradable phenolic polymers. This functionalization enhances the native value of the phenolic compound by releasing the phenolic moiety by hydrolysis or degradation of the compound. These phenolic compounds degrade under controlled environmental condition, in the body of an animal, for example a mammalian, including a human. Such functionalized phenolics can be prepared according to any recognized method, but the Williamson ether synthesis method is the preferred method. Limited research was done earlier[1] in this area.

Many examples of both the phenolics and the functionalization moieties have been shown to be safe and biocompatible. The new functionalized phenolic polymers can have controllable hydrolysis profiles, improved bioavailability, improved efficacy and enhanced functionality. These degradable phenolic polymers have many useful biomedical applications.

The glycolic, lactic, dioxanone, caprolactone moieties, have different hydrolysis or degradation rates and times over which they release the active phenolic moiety and thus do the functionalized phenolic compounds made from them. The species used for functionalization supplies the release time or range dictated by the application. Glycolic acid based compounds hydrolyze faster than p-dioxanone based, whereas lactic acid and caprolactone based compounds take much longer to hydrolyze than glycolic acid and p-dioxanone based compounds. This desired time range may be obtained by using a combination of functionalized phenolic compounds, that is, a blend of two or more functionalized compounds made from any two or more of the species glycolide, lactide, dioxanone and polydioxanone combined with one phenolic compound.

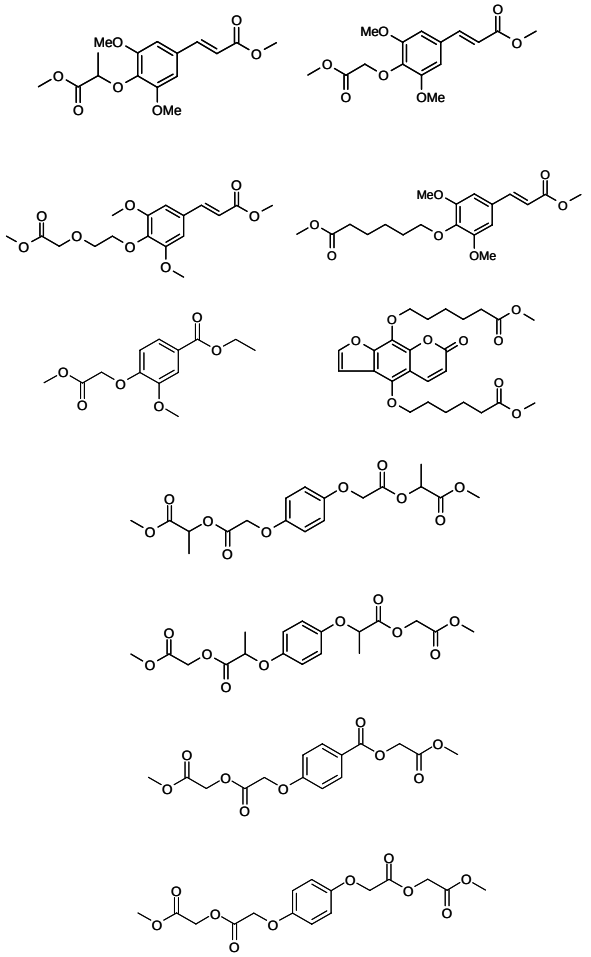

Figure 1. Novel functionalized phenolic monomers

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

REFERENCES

1. (a) Bezwada, et al, U.S. Patents, 4,510,295 & 4,532,928 (b) Shalaby and Jamiolkowski, U.S. patents, 4,689,424 & 4,435,590.