Novel Absorbable Radiation Stable Polymers from Functionalized Hydroquinone monomers

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INTRODUCTION

Sterilization of majority of commercially available absorbable medical devices is usually accomplished by the use of ethylene oxide, or gamma radiation (cobalt-60 radiation). Sterilization using ethylene oxide is costly and time-consuming. Furthermore, it leaves behind toxic ethylene oxide residues, which can have an adverse impact on functional performance and biocompatibility of the absorbable implantable medical devices. In contrast to this, sterilization using gamma radiation is simple, relatively less expensive, does not leave behind any sterilant-related toxic residues and hence is preferred as a sterilization method over ethylene oxide. However, the application of high-energy gamma radiation results in the degradation of base absorbable polymer material due to the generation of free radicals. Studies have suggested that radiation stability can be imparted to absorbable polymers by incorporating aromatic moieties in the polymer backbone chain. These aromatic moieties have the ability to act as free radical sinks, generating aromatic ring current, which safely dissipates the reactive energy of free radicals.

The objective of the current work is to develop radiation stable absorbable polymers with tunable hydrolytic degradation profiles. Since phenolic compounds contain aromatic rings, occur widely in nature, exhibit anti-oxidative, anti-inflammatory, anti-mutagenic properties and are used in numerous applications including pharmaceuticals and nutraceuticals, Hydroquinone, a diphenol containing aromatic ring substituted with two hydroxyl groups was chosen in the present study as the starting material. It was functionalized with safe and biocompatible molecules (e.g., glycolic acid, lactic acid, caprolactone, and p-dioxanone) to form functionalized hydroquinone monomers with tunable hydrolytic degradation profiles. The resulting functionalized hydroquinone monomers were then polymerized by condensation with diols to yield absorbable radiation stable polymers.

This paper describes the synthesis of functionalized hydroquinone monomers and absorbable polymers synthesized from these monomers. These polymers will be useful in a variety of biomedical applications including drug delivery, tissue engineering, stent coatings, stents, and implantable medical devices. Synthesis and characterization of monomers and polymers will be presented. *In Vitro* hydrolysis and the controllable hydrolysis profiles will be discussed during presentation.

RESULTS AND DISCUSSION

Functionalization of Hydroquinone. Hydroquinone molecule (Figure 1a) was conjugated with glycolic, lactic acid and caprolactone by Williamson etherification as shown in Figures 1(b)-(d) to form novel radiation stable and hydrolysable monomers. These monomers were then subjected to condensation polymerization with ethylene glycol to yield radiation stable absorbable polymers containing phenolic molecules in the backbone as shown in figures 2 (a)-(b). The monomers as well as the polymers in the present study will have different as well as controllable hydrolytic degradation rates. Glycolic acid functionalized hydroquinone monomers and corresponding polymers will hydrolyze faster than lactic acid and caprolactone functionalized monomers. and corresponding absorbable polymers. Furthermore, using different combinations of functionalization moieties enables us to control the hydrolytic degradation rates of monomers and polymers.

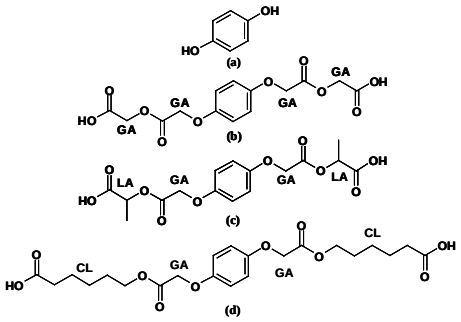

Figure 1. Functionalized hydroquinone monomers (a) hydroquinone (b) hydroquinone tetraglycolate (c) hydroquinone diglycolate dilactate and (d) hydroquinone diglycolate dicaprolactone where GA is glycolic acid, LA is lactic acid and CL symbolizes caprolactone unit.

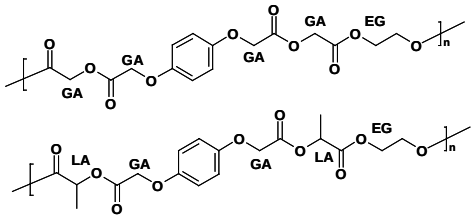

Figure 2. Radiation stable absorbable polymers derived from (a) hydroquinone tetraglycolate and (b) hydroquinone diglycolate dilactate.

CONCLUSIONS

These radiation stable absorbable polymers derived from hydroquinone will be used to prepare radiation stable absorbable sutures and coatings for implantable devices. In addition, these radiation stable absorbable polymers with tunable degradation profile can be very useful for controlled release of injectable drugs as well as in tissue engineering applications. The synthesis and characterization of novel hydrolysable functionalized hydroquinone monomers and corresponding radiation stable polymers will be presented in the meeting.

REFERENCES

1. Bezwada, Rao S., US Patent Application No. 2006/0173065 A1.
2. Bezwada, Rao S., World Patent Application No. WO2007053794A2.