

Absorbable Polymers from Functionalized Paracetamol

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Introduction:

The objective of our current work is to develop novel bioabsorbable polymers that incorporate drug molecules into the polymer backbone, which upon hydrolytic degradation yields safe and biocompatible products including the drug molecule so that the therapeutic value of the drug is delivered at the site of action over a period of time. In order to achieve the above-mentioned objective, we have developed novel absorbable polymers derived from functionalized paracetamol. Paracetamol is a common analgesic and antipyretic drug that is used for the relief of fever, headaches and other more severe pains resulting in lower dosages of additional NSAID or opiod analgesics to be used thereby minimizing over all side effects. The paracetamol molecule contains an amine and a hydroxyl group. In the present study, the drug paracetamol was conjugated with glycolic acid, lactic acid, p-dioxanone and caprolactone monomers from the hydroxyl. These monomers are the building blocks of majority of commercial degradable medical devices. The resulting functionalized paracetamol monomer was then polymerized to yield absorbable polymers.

Results/Discussion:

Functionalization of Paracetamol: The paracetamol molecule contains a protected amine and a hydroxyl functional group as shown in Figure 1 (a). In the present study, the hydroxyl functional group of the paracetamol was functionalized with glycolic acid, lactic acid and caprolactone moiety as shown in figure 1 (b), (c) and (d)

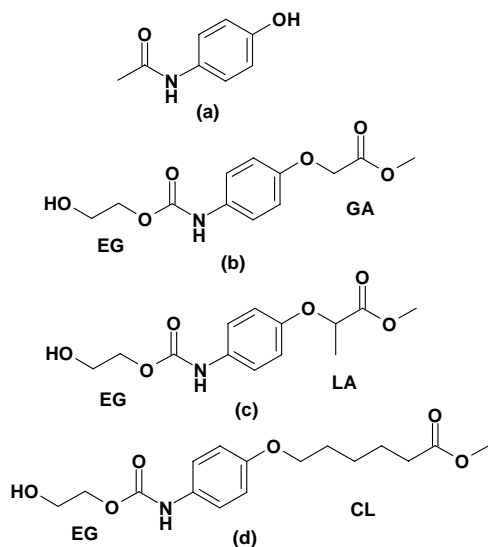


Figure 1. (a) Paracetamol (b) Glycolic acid^{GA} functionalized Paracetamol (c) Lactic acid^{LA} functionalized Paracetamol (d) Caprolactone^{CL} functionalized Paracetamol

respectively. The protected amine group of the paracetamol was functionalized with the ethylene glycol moiety as shown in figure 1(b)-(d). This functionalization resulted in the formation of novel absorbable AB type monomers derived from paracetamol which were then subjected to self-condensation polymerization to yield novel absorbable polymers containing paracetamol in the backbone as shown in figure 2(a)-(c). All the

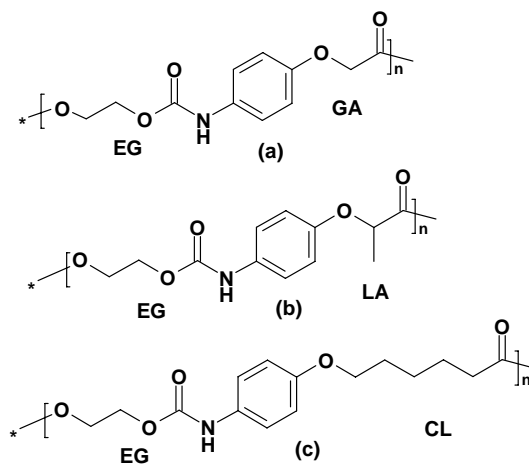


Figure 2 Absorbable polymers from functionalized Paracetamol

functionalized paracetamol monomers and the polymers derived from them were characterized using NMR spectroscopy. The details of the monomer and polymer synthesis and their characterization will be presented in detail in the meeting.

Conclusions: For the first time, absorbable polymers have been developed from functionalized paracetamol monomers. These polymers not only have controlled hydrolytic degradation profiles but are also anticipated to degrade into safe and biocompatible molecules. These polymers are an excellent candidates for drug delivery applications.

References:

- (1) (a) Bezwada, R.S. US Patent Publication No. 2006/0173065 (b) Bezwada, R.S. US Patent Publication No. 2006/0172983 (c) Bezwada, R.S. US Patent Publication No. 60/728823 (d) Bezwada, R.S. US Patent Publication No. 60/748789.
- (2) (a) Bezwada, R.S. PMSE Preprints 2006;51:825. (b) Bezwada, R.S. PMSE Preprints 2006;51:401. (c) Bezwada, R.S. PMSE Preprints 2006;51:399.