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Simultaneous HPLC-UV determination of lactic acid, glycolic acid, glycolide, lactide and ethyl acetate in monomers for producing biodegradable polymers

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Abstract

A simple, rapid high-performance liquid chromatographic (HPLC) method was developed for the simultaneous determination of glycolic acid, lactic acid, glicolide, lactide and ethyacetate in monomers for obtaining biopolymers. The separation was effected on the reversed-phase C18 column 250mm×4.6mm with particle size 5μ using a mobile phase mixture buffer and acetonitrile in a ratio 88:12 v/v and elution was isocratic at a flow-rate of 1.0 mL/min. The determinations were performed with a UV-Vis detector at 200 nm. The volume of the injected sample was 20 μL. Detection limits for acids and its dimers (glycolic acid, lactic acid, glicolide, lactide) and ethylacetate range between 82 and 182 ng/mL. The analytes are separated in 13 min. Recovery studies showed good results for all solutes (99–102%). The method is linear for all compounds over the concentration range tested, and shows good precision and accuracy, making it suitable for quantitation of acids and its dimers (glycolic acid, lactic acid, glicolide, lactide) and ethyl acetate in monomers.

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1. Introduction

Poly-lactic acid (PLA) is a biodegradable aliphatic polyester produced industrially both on a large and small scale. It

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is used for a wide variety of applications, ranging from biomedical applications to raw material for food packaging, bottles and consumables in general. Due to its excellent mechanical properties, permeability, transparency and environmental compatibility, in fact, PLA is a one of the most interesting polymeric candidate to replace on the market of non-biodegradable petroleum based synthetic polymers[1]. Recently, polymers based on lactic acid have received special attention in the field of medical applications because these polyesters degrade in the human body by hydrolysis of the ester backbone to non-harmful and non-toxic compounds. These compounds are also used in the production of implantable medical devices, in dental applications and, more recently, as scaffolds for autografted new skin, wound covers, anastomose systems and stents[2]. All of these devices can be loaded with a large number of different compounds such as drugs, pharmacological active principles, release modifiers and molecules suitable for Magnetic Resonance Imaging (MRI).

Nomenclature

LA - lactic acid;
GA - glycolic acid;
EA - ethyl acetate;
HPLC - high performance liquid chromatography;
RT - retention time;
RSD - relative standard deviation;
SD - standard deviation;
RE - relative error.

The synthesis of PLA and copolymers can follow three routes: (1) condensation polymerization, (2) azeotropic dehydrative condensation, and (3) ring-opening polymerization from the cyclic dimers. The third method, based on ring opening polymerization (ROP) of cyclic dimers is the only practical technique for producing pure high molecular weight polymers (Mw≥100,000) and the one that has been developed most widely for industrial-scale production. ROP also has the advantage that the chemistry and therefore the properties of the final polymer can be accurately controlled and tuned to requirements.

It is known that the impurities like lactic acid, glycolic acid, solvents in the monomer have a significant bearing on the molecular weight of PLA and copolymers. In addition, varying levels of water-soluble acid impurities are well known to exist in PLGAs, which can influence their solid-state stability, drug encapsulation efficiency, and drug release behavior. And it is important to determine the impurities content before polymerization, after storage and transportation. Impurities have been analysed in various matrices by various techniques. High performance liquid chromatography (HPLC) has been used to analyse short fatty acids[3,4] and lactide content in polymer[5]. Gas chromatography (GC) has been used for LA and GA analysis with the most reported methods[6,7,8,9,10] involving derivatization typically using t-butyldimethylsylil or oxidation to aldehyde. Derivatization is often the lengthy experiment and may not be appropriate for a high throughput laboratory. The potentiometric titration and pre-derivatization HPLC usage for the analysis of LA and GA has been reported, where the pre-derivatization HPLC method was developed for separation and quantification of water-soluble acid impurities and degradation products in PLGA and was compared with potentiometric titration by using tetrabutyl ammonium hydroxide[11]. Various other methods have already been reported for the detection and determination of LA and GA including amperometric lactate biosensors[12,13,14], electrophoresis[15,16], spectrophotometric method[16] and ion-exclusion HPLC.

However, these studies could not achieve simultaneous determination of glycolic acid, lactic acid, glycolide, lactide and ethyl acetate. The main purpose of this study was to develop a rapid, specific, precise and accurate HPLC method for analytical determination of acids and its dimers (GA, LA, glycolide, lactide) and ethyl acetate in monomers used in our project for obtaining PLA, PLGA and other copolymers. Thus, the validation of the analytical method is a necessary procedure and involves experimental studies of analytical parameters, in order to guarantee the analytical results. Some important parameters such as specificity and selectivity, linearity, accuracy and precision must be verified