Determination of solvent residues in biodegradable polyester, ethylene glycol, and propylene glycol copolymers

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Abstract: A method for the determination of residual solvents in glycolide propylene copolymer (PLGA) was established using a DB-624 (30 m x 530 μ m x 3.0 μ m) capillary chromatography column, hydrogen flame ionization detector (FID), and headspace injection. The experimental results show that the peak area and mass concentration of each solvent measured by this method exhibit a good linear relationship within the investigated concentration range. The recovery rate is between 98.54% and 99.50%, the precision RSD is less than 2%, and the quantitative limit is between 0.16 and 1.17 μ g/mL. This method is simple to operate, accurate in results, and has good reproducibility. It can be used for the simultaneous determination of residual solvents such as ethanol, acetone, dichloromethane, and ethyl acetate in PLGA.

Keywords: headspace gas chromatography; Capillary column; Biodegradable polyester; Ethylene glycol ester propylene glycol ester copolymer; Solvent residue

1.Introduction

PLGA copolymer is a biodegradable synthetic polymer with good biocompatibility and degradability [1-5]. It can be degraded into lactic acid and hydroxyacetic acid in the body, participate in human metabolism, and ultimately form carbon dioxide and water that are excreted from the body. Its degradation cycle can range from a few weeks to several years by adjusting the ratio of glycolide and lactide. It has been approved by the US FDA for clinical use and has been marketed in various products, such as Johnson&Johnson's multi strand suture Vicryl ® 、 Vicryl Rapid and PANACRYL, French Yipuzheng's Triptorelin PLGA microspheres, Chongqing Yongtong's PLGA postoperative absorbable anti adhesion film, etc. At present, PLGA has been widely studied for its applications in drug controlled release, tissue engineering scaffolds, absorbable sutures, anti adhesion membranes, bone implants, and ultrasound contrast agents, with enormous potential in the biomedical field.

The safety of PLGA as a biomedical material is crucial. We synthesized PLGA using propylene glycol and ethylene glycol as monomers through bulk ring opening polymerization. During the monomer purification and polymer refining processes, solvents such as ethyl acetate, dichloromethane, acetone, and ethanol were used, respectively. To ensure that the residual amount of PLGA was within the safe limit of use, it is necessary to establish a method for determining the residual solvent of PLGA. At present, solvent residue determination methods are mostly used in drugs, and there is little research on polymer materials. Therefore, this study used a capillary chromatography column and headspace injection method to determine the solvent residues of PL-GA75/25 and PLGA50/50 (with a molar ratio of 75:25 and 50:50 for lactide and glycolide, respectively), and established corresponding determination methods.

2 Materials and Methods

2.1 Instruments and reagents

Agilent 6890N gas chromatograph (FID detector); Agi lent 7697A automatic headspace sampler.

Ethanol, ethyl acetate, and dichloromethane are all chromatographically pure, produced by

the Chemical Branch of Shandong Yuwang Industrial Co., Ltd; Acetone, analytical pure, China National Pharmaceutical Group Chemical Reagent Co., Ltd; Dimethyl sulfoxide, chromatographically pure, China National Pharmaceutical Group Chemical Reagent Co., Ltd. PLGA 50/50 (molar ratio of lactide to glycolide 50: 50), self-made, batch numbers: 17061401, 17091302; PLGA 75/25 (molar ratio of lactide to glycolide 75:25), self-made, batch number: 17102401.

2.2 Chromatographic conditions

DB-624 capillary column (30 m x 530 μ m x 3.0 μ m), column temperature: initial temperature of 100 ℃, maintained for 5 minutes, then increased to 180 ℃ at a heating rate of 30 ℃/min; Injection port temperature: 200 ℃; Detector temperature: 250 ℃; Carrier gas: N2, flow rate of 3.0 mL/min; The diversion ratio is 10:1; Top space heater temperature: 100 ℃; Quantitative valve temperature: 110 ℃; Transmission line temperature: 120 ℃; Balance time of headspace bottle: 20 minutes; Injection volume: 1 mL.

2.3 Preparation of standard solution

Take 1.0 g of ethanol, acetone, and ethyl acetate each, accurately weigh them, and place them in the same 100 mL volumetric flask; Take another 1.2 g of dichloromethane, accurately weigh it, dissolve it in dimethyl sulfoxide and make up to 100 mL, accurately measure 10 mL, place it in the aforementioned volumetric flask, dilute with dimethyl sulfoxide and make up to volume, as the standard storage solution.

Accurately measure 5 mL of standard stock solution and place it in a 50 mL volumetric flask. Dilute with dimethyl sulfoxide and make up to volume as the standard solution.

2.4 Sample solution preparation

Take 1.0 g of glycolide propylene copolymer, accurately weigh it, place it in a headspace bottle, add 5 mL of dimethyl sulfoxide and seal it. Wait for complete dissolution and use it as the sample solution.