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博 士 学 位 论 文

脂肪族聚酯生物材料的亲水性增强改性研究

Study of Hydrophilicity Enhancement of Aliphatic Polyester Biomaterials

姜元芹

指导教师姓名：任磊　教授/博导
专　业　名　称：高分子化学与物理
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摘 要

脂肪族聚酯不仅具有良好的生物相容性，而且可生物降解，能参与体内正常代谢的低分子量化合物或单体。脂肪族聚酯一般为结晶性聚合物，降解周期过长，难以调节，其降解一般通过其主链酯键的水解进行，其降解速度和降解程度取决于其自身的性质，如亲水性、结晶性等。此外，脂肪族聚酯的一般为非亲水性材料，这使得细胞难以附着、亲和能力低。本论文针对上述问题，以增强脂肪族聚酯材料的亲水性和降低其结晶度为目的，通过共混法成功地制备了多种脂肪族聚酯可降解材料，并研究了共混组份间的相容性和材料的亲水性。本论文的主要研究工作如下：

（1）通过热聚合法合成了聚己内酯（PCL），并通过沉淀分级法制备了窄分散的级分。通过溶液浇铸法，成功制备了PCL和聚乙二醇（PEG）的共混膜。采用傅里叶红外光谱（FTIR）、热失重分析（TGA）、示差扫描量热（DSC）和X-射线衍射（XRD）分析研究各组份之间的相互作用。结果显示PCL和PEG二组分间存在一定程度的相容性，并由于氢键相互作用，使得共混材料中PCL的结晶度降低。PCL/PEG共混材料经扫描电镜（SEM）结果观察，显示PCL/PEG共混材料表面和内部多孔网路结构，且这种结构随PEG含量的增加而增加。将模型药物布洛芬（IBU）载入上述共混物中制成药片， IBU能从其中迅速释放出来，且释放速率随PEG在共混材料中含量增加而增大。

（2）采用三氟乙酸为共溶剂溶解聚乳酸（PLA）和壳聚糖（CS），通过溶液共混、浇铸制备了二者的共混材料。结果显示，共混材料中PLA与CS具有一定程度的相容性。即PLA/CS在CS含量为20%或80%时，PLA/CS表现出相容而未发生相分离；但在PLA/CS组成相近时，将出现一定程度的微相分离结构。水接触角和吸水率测定结果显示，在共混入CS后， PLA材料的亲水性显著增强，随CS含量提高逐渐转变成亲水性材料，且吸水率大幅提高、吸水速率也得到提高。

（3）将PLA或PCL溶解于氯仿中，并加入CS和PVA的醋酸水溶液中，剧烈搅拌后能形成均匀且较为稳定的乳液。乳液经溶剂挥发后，成功制备了PLA/ CS/ PVA和PCL/ CS/ PVA两种三元共混材料。FTIR、DSC结果显示，共混材料中组份

间具有较强的相互作用，具有一定的相容性，使PLA或PCL的熔点、结晶度降低。SEM结果发现，三元PLA/ CS/ PVA和PCL/ CS/ PVA共混材料均为较致密的均匀结构。由于亲水性PVA的引入，使所得PLA/ CS/ PVA和PCL/ CS/ PVA共混材料的亲水性大大增强，水接触角分别为51°和46°。同时，水溶性聚乙烯醇（PVA）的存在，也使材料的吸水速率和吸水率大大提高。

综上所述，通过便捷的溶液共混和乳液共混并增溶，可将亲水性或水溶性的PEG、CS和PVA引入脂肪族聚酯体系，制备可降解的脂肪族聚酯基复合材料，从而使脂肪族聚酯的结晶度降低，并提高其亲水性和吸水率。

关键词：脂肪族聚酯；生物医用材料；共混；改性

Abstract

Aliphatic polyesters are extensively investigated in the biomedical material fields due to their satisfactory biocompatibility as well as high biodegradability, which are based on their metabolizing and without accumulation after implantation in vivo. In this work, the developments of using aliphatic polyesters as biomedical materials are briefly reviewed, and the degradations of the aliphatic polyesters are introduced. The degradation of aliphatic polyesters usually takes place by hydrolyzing of their ester bonds along the polymer chains, and the degradation rate is normally determined by the innate characters of aliphatic polyester such as its hydrophilicty and crystallinity, which are of key importance for the biomedical materials prepared from aliphatic polyesters. Aliphatic polyesters are materials with strong hydrophobicity, which is not of benefit to the adhersion and affinity of cells onto the aliphatic polyester materials. Moreover, aliphatic polyesters are in many cases with high crystallinity, which makes very long degradation time and uncontrolable degradation rate of the accordingly obtained materials. In order to improve the hydrophilicity and to decrease the crystallinity, hydrophilic polymers have been blended with aliphatic polyesters in solution, and the compatibility of the components and the enhancement of hydrophilicty of thus prepared biomedical materials were investigated in this work, which are summarized as following:

(1) Poly(ε-caprolactone)(PCL) was thermally polymerized, and then was fractionated by precipitation. Thus prepared PCL was co-dissolved in dichloromethane with low-molecular weight hydroxyl terminated polyethylene glycol (PEG). By casting the obtained mixture solution and evaporating solvent, PCL/PEG blend films have successfully prepared. The interaction of PCL and PEG was measured by means of Fourier transform infrared (FTIR) spectra; thermogravimetric analyses (TGA), differential scanning calorimetry (DSC) analyses and X-ray diffraction (XRD) patterns of the blend films, and the results indicate partial compatiablity of the two components and the derease in crystallinity of the blend material. The miscibility between PCL and PEG is resulted from their interaction,

which might be hydrogen bonding between carbonyl groups of PCL and hydroxyl groups of the low-molecular weight PEG. Scanning electron microscope (SEM) images of the blend films reveal porous network structures for their surfaces and for their inner parts, and the porous structure becomes more pronounced with the increase of PEG in the blend film. Ibuprofen (IBU) was used as the model drug to test the drug release behavior for the PCL/PEG blend matrices. The results show that IBU could be released from the blend tablets rapidly, and the release rate increases with PEG content. Analysis of the release profiles indicates PCL erosion control release mechanism of pure PCL tablet, but drug diffusion control of the blend tablet, because PEG can absorb water to allow water feasible to diffuse into drug core and dissolve drug. Therefore, the inter-connected channels in the blend matrices and the hydrophilic nature of PEG contribute to the improvement of the IBU release rate. The research indicates that drug release rate from PCL based material could be efficiently improved by addition of small amount of hydrophilic low-molecular-weight PEG.

(2) Polylactic acid (PLA) and chitosan (CS) were co-dissolved in trifluoroacetic acid (TFA), and then was casting to evaporate THF at ambient condition to prepare blend films. The FTIR and DSC analyses indicate partial miscibility of PLA and CS in the blend films, which results from hydrogen bonding between the amine and hydroxyl groups of CSand the carbonyl groups PLA. The miscibility of the components results in decrease of the cystalinity and melting temperature of PLA. It has been found that there is no obvious phase separation in blend films of 20% and 80% CS content. With the increase of CS content in the blend film, the water contact angle of the blend film dereases, while its water sorption and water sorption rate increases markedly, indicating hydrophobic to hydrophilic transition of the blend material. Therefore, the hydrophilicity of PLAbased material can be easily enhanced by blending with CS.

(3) Stable emulsions have been prepared by energetically stirring PLA or PCL chloroform solution with CS/polyvinyl alcohol (PVA) acitic acid mixture solution. After evaporation of solvent, ternary blends of PLA/CS/PVA and PCL/CS/PVA have been respectively prepared. The FTIR and DSC analyses indicate partial miscibility of

the components in the blend films, which result in decrease of the cystalinity and melting temperature of PLA and PCL. The SEM observations indicate dense structures of the ternary blends, which are different from the phase separation of the binary blends of PLA/CSand PCL/CS prepared by the same emulsion manner. The results suggest that PVA acts as a compatilizer to improve the miscibility of PLA or PLA with CS, leading to more even distributions of the components. Due to the introduction of the water soluble PVA, the water contact angles derease to 51° and 46° of the PLA/CS/PVA and PCL/CS/PVA ternary blends, respectively, meaning great enhacement in hydrophilicity of the aliphatic polyester materials. At the same time, the water sorption and water sorption rate increases evidently because of the presence of PVA in the blends.

(4) It is facile to introduce hydrophilic or water soluble polymers such as PEG, CS or PVA into aliphatic polyester materials by blending and emulsification. Thus prepared materials retain biocompatibility and biodegradability. Due to the interaction between the introduced hydrophilic polymers and aliphatic polymer, the cystalinity of the aliphatic polymer is suppressed, while the hydrophilicity and water sorption of the blend are greatly enhanced. Therefore, it is anticipated that the materials prepared in this work would have great potential applications in field of tissue engineering.

Keywords: aliphatic polyesters; biomedical materials; blend; modification

第一章 绪论

1.1 引言

全世界经济的高速发展和人们对生活水平要求的不断提高，对用于各行各业的材料也提出了新的更为严格的要求。与钢材、木材和水泥并列为四大支柱材料的塑料，也得到了长足的发展，目前其产量已超过 2 亿吨[1]，并应用于国民经济各部门以及人民生活的各个方面。但塑料制品在在改善人们生活品质的同时，也带来了引人注目的问题：塑料废弃物引发的环境污染和对化石资源的严重依赖性问题[1]。因此，人们开始寻找、利用廉价并丰富的天然可再生资源如淀粉、纤维素、蛋白质等弥补甚至替代以化石资源为原料的高分子材料，以及开发可降解塑料或研究塑料回收、再利用技术。

可降解塑料是指在加工、贮存和使用过程中，塑料各项性能要相对稳定且满足使用要求，但在使用后能降解成对环境无害的物质。根据降解的机理，可降解塑料一般分为以下几类：（1）生物降解塑料；（2）光降解塑料；（3）氧化降解塑料和（4）水解降解塑料。但是，可降解塑料的降解通常是上述降解机理的多项组合，如生物降解塑料通常还涉及化学降解和水解降解。在 20 世纪后期，为解决“白色环境污染”问题，人们投入了大量的精力和热情研发光降解塑料并获得了一定成绩。目前，生物可降解塑料尤其是以脂肪族聚酯为代表的可生物降解高分子材料更为引人注目，成为研究热点[2-16]。

1.2 脂肪族聚酯

1.2.1 脂肪族聚酯

脂肪族聚酯可生物降解高分子材料是指在一定的时间和适当的自然条件下能够被微生物（如真菌、细菌、藻类等）或其分泌物在酶或化学分解作用下发生降解的聚合物材料。脂肪族聚酯的降解产物为低分子量化合物或单体，且这类降