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论文

温敏性PCL-PEG-PCL水凝胶的合成、表征及蛋白药物释放

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摘要:

考察了温敏性PCL-PEG-PCL水凝胶中聚乙二醇(PEG)及聚己内酯(PCL)不同嵌段组成对其溶胶-凝胶相转变温度以及亲水性药物(牛血清白蛋白, BSA)释放速率的影响. 采用开环聚合法, 以辛酸亚锡为催化剂、PEG1500/PEG1000为引发剂, 与己内酯单体发生开环共聚, 合成了一系列具有不同PEG和PCL嵌段长度的PCL-PEG-PCL型三嵌段共聚物. 通过核磁共振氢谱及凝胶渗透色谱对其组成、结构及分子量进行了表征. 共聚物的溶胶-凝胶相变温度由翻转试管法测定. 利用透射电镜、核磁共振氢谱及荧光探针技术证实了该材料在水溶液中胶束的形成. 以BSA为模型蛋白药物, 制备载药水凝胶, 利用microBCA法测定药物在释放介质中的浓度, 研究其体外释放行为. 实验结果表明, 共聚物的溶胶-凝胶相变温度与PCL及PEG嵌段长度紧密相关, 即在给定共聚物浓度情况下, 固定PEG嵌段长度而增加PCL嵌段长度, 会导致相变温度降低; 而固定PCL嵌段长度而增加PEG嵌段长度, 其相变温度相应升高. 水凝胶中蛋白药物的释放速率与疏水的PCL嵌段长度无关, 而与亲水的PEG嵌段长度密切相关, 即PEG嵌段越长, 蛋白药物释放越快.

关键词: PCL-PEG-PCL共聚物; 温度敏感; 水凝胶; 凝胶相变温度; 蛋白药物释放

Synthesis, Characterization and Protein Drug Release of Temperature-Sensitive PCL-PEG-PCL Hydrogel

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Abstract:

The effect of PEG and PCL composition of thermosensitive PCL-PEG-PCL hydrogels on Sol-gel transition temperature and release rate of bovine serum albumin(BSA) were investigated. A series of thermosensitive PCL-PEG-PCL triblock copolymers with different PEG and PCL block lengths were synthesized *via* ring-opening polymerization of *ε*-CL using PEG1500/PEG1000 as the initiator and Sn $(Oct)_2$ as the catalyst. Their composition, structure, and molecular weight were characterized *via* ^1H NMR and GPC techniques. The Sol-gel transition temperature was determined with the test tube inverting method. TEM, ^1H NMR, and fluorescence probe technique were employed to identify formation of micelles of the triblock copolymers in aqueous solution. BSA was used as a model protein drug. Hydrogels of these PCL-PEG-PCL triblock copolymers loaded with BSA were prepared for *in vitro* release study, and BSA concentration in the released sample was determined with microBCA method. The effect of PCL and PEG block lengths on Sol-gel transition temperature and release rate of BSA was also discussed. The results obtained indicated that the Sol-gel transition temperature of copolymers was related to block lengths of PCL and PEG, increasing the PCL length at a fixed PEG central block led to a lower transition temperature at a given copolymer concentration, while with the enhancement of the PEG length at a similar hydrophobic PCL length, the transition temperature increases. And the protein release rate was independent of the hydrophobic PCL length, whereas the longer PEG length, the lower protein release rate.

Keywords: PCL-PEG-PCL copolymer; Temperature-sensitive; Hydrogel; Sol-gel transition temperature; Controlled release of protein drug

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参考文献:

[1]Sanders L. M.. Eur. J. Drug Metab Pharmacokinet[J], 1990, 15(2): 95—102
[2]Singh S., Webster D. C., Singh J.. International Journal of Pharmaceutics[J], 2007, 341: 68—77
[3]Ruel-Gariépy E., Leroux J. C.. European Journal of Pharmaceutics and Biopharmaceutics[J], 2004, 58(2): 409—426
[4]Yu T., Singh J.. International Journal of Pharmaceutics[J], 2009, 365: 34—43
[5]Richter A. W., Akerblom E.. Int. Arch. Allergy Appl. Immunol.[J], 1983, 70(2): 124—131
[6]Marcotte N., Polk A., Goosen M. F.. J. Pharm. Sci.[J], 1990, 79(5): 407—410
[7]Hwang M. J., Suh J. M., Bae Y. H., et al.. Biomacromolecules[J], 2005, 6: 885—890
[8]Gong C. Y., Shi S., Dong P. W., et al.. International Journal of Pharmaceutics[J], 2009, 365: 89—99
[9]Loh X. J., Goh S. H., Li J.. Biomacromolecules[J], 2007, 8: 585—593
[10]Ge H. X., Hu Y., Jiang X. Q., et al.. Journal of Pharmaceutical Sciences[J], 2002, 91(6): 1463—1473
[11]Wilhelm M., Zhao C. L., Wang Y. C., et al.. Macromolecules[J], 1991, 24: 1033—1040
[12]LIN Hao(林浩), TIAN Hua-Yu(田华雨), SUN Jing-Ru(孙敬茹), et al.. Chem. J. Chinese Universities (高等学校化学学报)[J], 2006, 27(7): 1385—1388
[13]Ryu J. G., Jeong Y. I., Kim I. S., et al.. International Journal of Pharmaceutics[J], 2000, 200(2): 231—242
[14]Qiao M. X., Chen D. W., Hao T. N., et al.. International Journal of Pharmaceutics[J], 2007, 345(1/2): 116—124
[15]Yu L., Chang G. T., Zhang H., et al.. Journal of Polymer Science Part A: Polymer Chemistry[J], 2007, 45(6): 1122—1133

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