高分子学报 2005 (4): 524-528 ISSN: 1000-3304 CN: 11-1857/O6

论文

可生物降解肝素钠/两性壳聚糖复合物用于蛋白药物pH响应释放研究

汪一娟, 蒋宏亮, 胡应乾, 朱康杰

浙江大学高分子科学与工程系; 浙江大学高分子科学与工程系 杭州

收稿日期 2004-3-26 修回日期 2004-6-25 网络版发布日期 接受日期

摘要 制备了一类可生物降解肝素钠两性壳聚糖复合物(HPACS),并探索将其用于蛋白药物pH响应释放.两性壳聚糖由壳聚糖与丙烯酸加成反应得到,丙烯酸取代度可通过丙烯酸壳聚糖投料比调控;用胶体与pH浊度滴定研究了肝素钠与两性壳聚糖的复合作用,发现两组分在一定pH范围内能通过静电相互作用形成复合物,复合转变临界pH(pHΦ)与两性壳聚糖中丙烯酸取代度有关,取代度越低,pHΦ值越高.以牛血清白蛋白(BSA)为模型,测定了其在复合物中包埋及不同pH介质中的释药行为.结果表明,BSA可以在非常温和条件下有效包埋于复合物中,包埋率接近100%;BSA从复合物中释放具有很高的pH响应性,释放转变在很窄的pH范围内(<0.4pH单位)完成,释放转变临界pH(pH′Φ)可由两性壳聚糖中丙烯酸取代度调控.复合物形成和蛋白质释放在对pH依赖性上存在很好的相关性.同时还发现,在中性介质中(pH7.4),复合物对BSA具有很好的缓释作用,BSA持续释放时间可达15天左右.

关键词 pH响应水凝胶 聚电解质复合物 蛋白药物 聚电解质/蛋白质复合物

分类号

BIODEGRADABLE HEPARIN/AMPHOLYTIC CHITOSAN COMPLEXES FOR pH-SENSITIVE RELEASE OF PROTEINS

WANG Yijuan,JIANG Hongliang,HU Yingqian,ZHU Kangjie

Department of Polymer Science and Engineering; Zhejiang University; Hangzhou 310027

Abstract A series of biodegradable heparin/ampholytic chitosan (HP/ACS) complexes were developed for pH- sensitive release of protein drugs. ACS was synthesized by using acrylic acid (AA) and chitosan,and the substitution degree (SD) of AA can be modulated by the AA/chitosan feed ratio. The complexation between heparin and ACS was studied by colloid and turbidity titration. It was found that HP and ACS can form complexes within a certain pH range and the critical pH value for complexation (pH_{Φ}) is related to the SD of AA. The larger the SD,the higher the pH_{Φ} value. Bovine serum albumin (BSA) was selected as a model protein,and its entrapment and release behavior from HP/ACS complexes were investigated. The results show that the entrapment efficiency of BSA is very high(～100％),and the BSA release is extremely pH-dependent. The transition of BSA release can occur within a rather narrow pH range(<0.4 unit). The critical pH value for the transition(pH'_{Φ}) can also be modulated by SD. It seems that the BSA release transition is correlated with HP/ACS complexation. In addition. the sustained release of BSA from the complex can be achieved at pH 7.4 and the releabe duration can be up to 15 days.

Key words pH-Responsive hydrogel Polyelectrolyte complex Protein Polyelectrolyte/Protein complex

DOI:

通讯作者 蒋宏亮