

摘要

本次论文的主题是以聚乳酸作为高分子药物载体，通过和小分子的抗肿瘤药物相连接，最终合成了聚乳酸靶向抗肿瘤药物。该药物具有靶向功能，能够准确地到达肿瘤部位，而且还可以在人体细胞内缓慢释放。既提高了疗效，又降低了对人体的毒副作用。

本次实验采用传统的阴离子开环聚合引发丙交酯开环。磺胺嘧啶可以在肿瘤部位富集，为提高药物的靶向性，先合成带靶向基团（磺胺嘧啶）的阴离子引发剂，再用相转移催化法合成氟尿嘧啶-聚乳酸载体。最后将载体和 5-氟尿嘧啶-1-基乙酸通过酯化反应合成目标产物。先用红外光谱法、XRD、DSC 对 SF-PLA 的结构进行表征。然后用 SEM、红外光谱等对目标产物的结构形态进行表征，并通过紫外分光光度计获得回归方程，计算药物的包封率和载药量。最后配制不同 PH 的缓冲液进行体外检测其释药性能，用傅里叶分光仪测定，观察出现的峰。

对比 SF-PEG 和 SF-PLA 两种高分子载体，其 Tm、Tg、结晶性相差不太多，但 SF-PEG 的分子量不好控制，而 SF-PLA 的分子量在 3000 左右，考虑到人体代谢情况，本次实验选择聚乳酸作为高分子载体。而对于化学合成法和溶剂法制备得到的高分子药物，聚乳酸微球的最佳载药量为 35.77%，最高释药率高达为 95%；SF-PEG-FU 的载药量为 3.27%，但聚乳酸微球的表面比较粗糙。所以综合考虑，本次实验以聚乳酸为载体，通过化学合成法制备目标药物。

关键词：靶向药物；聚乳酸；5-氟尿嘧啶；磺胺嘧啶

Abstract

The theme of this paper is polylactic acid as a high molecular drug carrier. Through the connection with small molecular anti-tumor drugs, the targeted anti-tumor drugs of polylactic acid are finally synthesized. The drug has targeted functions, can reach the tumor site accurately, and can also be released slowly in human cells. It not only improves the curative effect, but also reduces the toxic and side effects on human body.

In this experiment, the traditional anionic ring-opening polymerization was used to initiate lactide ring-opening. Sulfadiazine can be enriched in tumor sites. In order to improve drug targeting, anion initiator with targeted group (sulfadiazine) was first synthesized, and then fluorouracil - PLA carrier was synthesized by phase transfer catalysis. The target product was synthesized by esterification of 5-fluorouracil -1- acetic acid. The structure of SF-PLA was characterized by INFRARED spectroscopy, XRD and DSC. Then, SEM and IR spectra were used to characterize the structure and morphology of the target products, and the regression equation was obtained by uv spectrophotometer to calculate the encapsulation rate and drug loading. Finally, different PH buffers were prepared to detect the drug release performance in vitro, and the peaks were observed.

Compared with SF-PEG and SF-PLA, the T_m , T_g and crystallinity of sF-PEG and SF-PLA were not too different, but the molecular weight of SF-PEG was not easy to control, while the molecular weight of SF-PLA was around 3000. Considering the metabolism of human body, PLA was selected as the polymer carrier in this experiment. For the polymeric drugs prepared by chemical synthesis and solvent method, the optimum drug load and the highest drug release rate of PLA microspheres were 35.77% and 95% respectively. The drug loading of SF-PEG-FU was 3.27%, but the surface of PLA microspheres was rough. Therefore, taking polylactic acid as the carrier, this experiment prepared the target drug through chemical synthesis.

Keywords: targeted drugs; Polylactic acid; 5-fluorouracil; sulfadiazine

目 录

1	引言	1
1.1	靶向高分子药物的概述及现状	1
1.1.1	靶向药物的概述	1
1.1.2	靶向药物的研究发展现状	2
1.1.3	靶向药物的临床优势与开发意义	2
1.1.4	5-氟尿嘧啶衍生物在靶向药物传递系统的研究进展	3
1.1.5	聚乳酸及其共聚物在靶向药物传递系统的研究进展	5
1.2	可用于制作靶向高分子药物的材料	8
1.2.1	常见的高分子载体药物	8
1.2.2	靶向基团的选择	9
1.2.3	聚乳酸材料的优点	9
1.3	聚乳酸微球的制备方法	10
1.4	本实验的目的和方法	12
2	实验原理	13
2.1	阴离子引发丙交酯开环聚合机理	13
2.2	5-氟尿嘧啶作用机理	13
3	实验部分	15
3.1	实验药品及仪器	15
3.1.1	实验药品	15
3.1.2	实验设备及仪器	16
3.2	聚乳酸靶向高分子药物的合成	16
3.2.1	他人的实验步骤及测试方法	16
3.2.2	合成磺胺嘧啶钾盐	16
3.2.3	2-氯乙酰胺基乙醇的制备	17
3.2.4	带靶向基团的阴离子引发剂的合成	17
3.2.5	引发丙交酯开环聚合	17
3.2.6	5-氟尿嘧啶-1-基乙酸的合成	18
3.2.7	靶向抗肿瘤药物的合成	18

以上内容仅为本文档的试下载部分，为可阅读页数的一半内容。如要
下载或阅读全文，请访问：

<https://d.book118.com/038077115062006076>