

论文

星点设计结合效应面法优化声学脂质微泡的制备

赵应征^{1*#};鲁翠涛^{1#};梅兴国

1. 温州医学院, 浙江 325035; 2. 军事医学科学院毒物药物研究所, 北京 100850

摘要:

声学微泡是近年发展起来的药物靶向递送系统, 利用超声波作用促进药物或基因定位释放到细胞或组织中。本文利用星点设计(CCD)结合效应面法(RSM)优化声学脂质微泡制备条件。蛋黄磷脂、Tween 80和聚乙二醇1500是影响2~8 μm微泡浓度的主要因素。本文应用星点设计综合考察这些因素, 利用效应面优化法得到最佳处方。实验评价指标为2~8 μm粒径的微泡浓度。采用多元二次方程对实验结果进行拟合, 从而产生三维效应曲面图, 最佳处方条件可从三维效应曲面的顶点得到。优化实验得到的最佳处方进行加速试验, 考察稳定性。通过体内造影效果实验, 研究本品的声学效应, 并与国外上市产品SonoVue 进行对照。结果表明, 3个考察因素对2~8 μm微泡浓度均有影响, 最佳处方配比为: 蛋黄磷脂8.35 mg, Tween 8021.68 mg和聚乙二醇1500201 mg。所制备的2~8 μm微泡浓度平均值达到 $8.60 \times 10^9 \cdot \text{mL}^{-1}$ 。加速试验结果显示脂质微泡物理稳定性良好。本品最佳处方体内造影强度(相对强度)和持续时间分别为 4.47 ± 0.15 和 $(302 \pm 7)\text{s}$, 与国外上市产品SonoVue [4.28 ± 0.13 和 $(309 \pm 8)\text{s}$]无明显差异。星点设计结合效应面法筛选出的声学脂质微泡浓度高, 物理稳定性和声学造影效果好。

关键词: 声学脂质微泡 星点设计 效应面法 造影

Optimization of the preparation of sonogenic phospholipids-based microbubbles by using central composite experimental design and response surface methodology

ZHAO Ying-zheng LU Cui-tao MEI Xin-guo

Abstract:

Sonogenic microbubble agent is a newly developed drug targeting delivery system, which uses ultrasonic beam to enhance the delivery of drug and gene to targeted cells and tissues. In this paper, the preparation of sonogenic phospholipids-based microbubbles was optimized by using central composite experimental design (CCD) and response surface methodology (RSM). Hydrogenated egg phosphatidylcholine (EPC), Tween 80 and polyethylene glycol 1500 (PEG 1500) were important components affecting the concentration of 2-8 μm microbubbles in the preparation. The combined effects of these three factors were analyzed by CCD and optimized by RSM. Evaluation variable was the concentration of 2-8 μm microbubbles. Overall desirability was fitted to a second-order polynomial equation, through which three dimensional response surface graphs were produced. Optimal experimental conditions were selected from the stationary point of the response surfaces. The stability of the sonogenic phospholipids-based microbubbles by the optimal formulation was investigated by accelerated experiment. The contrast effect *in vivo* of the optimal formulation was investigated. Foreign market product SonoVue was used as the control. From the results, all the three factors had positive effects on the concentration of 2-8 μm microbubbles. The optimal condition in the preparation of phospholipids-based microbubbles was obtained as following: EPC8.35 mg, Tween 8021.68 mg and PEG 1500201 mg. The mean value of the concentration of 2-8 μm microbubbles in rechecking experiment reached $8.60 \times 10^9 \cdot \text{mL}^{-1}$. From the accelerated experiment, phospholipids-based microbubbles showed good physical stability. The intensity (relative unit) and duration of the contrast effect by the optimal formulation were 4.47 ± 0.15 and $(302 \pm 7)\text{s}$ respectively, which showed little difference with foreign market product SonoVue [4.28 ± 0.13 , $(309 \pm 8)\text{s}$]. The optimal formulation selected by CCD and RSM showed high microbubble concentration, good physical stability and effective sonogenic contrast effect.

Keywords: central composite design response surface methodology contrast effect sonogenic phospholipids-based microbubble

收稿日期 2008-02-29 修回日期 网络版发布日期

DOI:

基金项目:

扩展功能

本文信息

- ▶ Supporting info
- ▶ PDF(988KB)
- ▶ [HTML全文]
- ▶ 参考文献

服务与反馈

- ▶ 把本文推荐给朋友
- ▶ 加入我的书架
- ▶ 加入引用管理器
- ▶ 引用本文
- ▶ Email Alert
- ▶ 文章反馈
- ▶ 浏览反馈信息

本文关键词相关文章

- ▶ 声学脂质微泡
- ▶ 星点设计
- ▶ 效应面法
- ▶ 造影

本文作者相关文章

- ▶ 赵应征1#
- ▶ 鲁翠涛1#
- ▶ 梅兴国

PubMed

- ▶ Article by
- ▶ Article by
- ▶ Article by

通讯作者: 赵应征,鲁翠涛

作者简介:

参考文献:

本刊中的类似文章

文章评论 (请注意:本站实行文责自负, 请不要发表与学术无关的内容!评论内容不代表本站观点.)

反馈人	<input type="text"/>	邮箱地址	<input type="text"/>
反馈标题	<input type="text"/>	验证码	<input type="text" value="8485"/>

Copyright 2008 by 药学学报