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论文

问题肝素中多硫酸软骨素杂质的柱前衍生高效液相色谱分析

赵峡, 李广生, 于广利, 王金霞, 王皓, 孙淑萌, 郑晨

中国海洋大学医药学院, 海洋药物教育部重点实验室, 青岛 266003

摘要:

基于肝素和多硫酸软骨素(OSCS)在单糖组成上的差别, 建立了可用于肝素中OSCS检测的柱前衍生高效液相色谱法. 采用3 mol/L三氟乙酸, 将受污染的问题肝素在110 ℃下充氮封管水解4 h, 在碱性条件下与1-苯基-3-甲基-5-吡唑啉酮进行衍生化反应, 再采用C_{18}反相色谱柱, 以0.1 mol/L磷酸盐(pH=6.7)缓冲液/乙腈(体积比82∶18)为流动相, 在流速1.0 mL/min、柱温25 ℃及紫外检测波长245 nm的条件下进行液相色谱分析. 结果表明, 肝素和OSCS的单糖色谱峰具有良好的分离度, 测得2批问题肝素中OSCS杂质的质量分数分别为19.6%和28.3%. 该方法具有良好的精密度和重现性, 易于推广, 适合于肝素中OSCS杂质的检测, 并可用于硫酸软骨素A和C与硫酸软骨素B的区分和鉴别.

关键词: 肝素; 多硫酸软骨素; 高效液相色谱; 1-苯基-3-甲基-5-吡唑啉酮

Analysis of Oversulfated Chondroitin Sulfate in Contaminated Heparin by Precolumn Derivatization High Performance Liquid Chromatography

ZHAO Xia*, LI Guang-Sheng, YU Guang-Li, WANG Jin-Xia, WANG Hao, SUN Shu-Meng, ZHENG Chen

Key Laboratory of Marine Drugs, Ministry of Education, School of Medicine and Pharmacy, Ocean University of China, Qingdao 266003, China

Abstract:

Based on the monosaccharide composition difference between heparin and OSCS, a simple and quantitative high performance liquid chromatography method has been established to determine OSCS present in contaminated heparin in this paper. After degradation of contaminated heparin by 3 mol/L trifluoroacetic acid(TFA) at 110 ℃ for 4 h, the monosaccharides were derivatized with 1-phenyl-3-methyl-5-pyrazolone(PMP), and separated on a C_{18} reversed phase column with a mobile phase of 0.1 mol/L phosphate buffer-acetonitrile(82∶18, volume ratio) at a column temperature of 25 ℃. The flow rate was 1.0 mL/min and the detection wavelength was 245 nm. There is a good separation between the peaks of monosaccharide-PMP derivatives of heparin and OSCS under the chromatographic conditions, and the two lots of contaminated heparin were found to contain 19.6% and 28.3% OSCS, respectively. This method is easy to apply and suitable for the determination of OSCS contaminant in heparin with high accuracy, reproducibility and sensitivity.

Keywords: Heparin; Oversulfated chondroitin sulfate; High performance liquid chromatography; 1-Phenyl-3-methyl-5-pyrazolone

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通讯作者: 赵峡, 男, 博士, 副教授, 主要从事糖类药物化学研究. E-mail: zhaoxia@ouc.edu.cn

作者简介:

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