

研究论文

## 高效液相色谱-串联质谱法分离鉴定单唾液酸四己糖神经节苷脂中的杂质

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**摘要** 用高效液相色谱法(HPLC)分析了单唾液酸四己糖神经节苷脂(GM1)药物的冻干粉、中间体和注射液各6个批号的样品,以期查找出采用不同工艺生产的成品中造成临床副反应的可能杂质。在用HPLC对多个批号GM1成药的对比分析中,发现某个批号的GM1干粉中多出2个杂质峰,其保留时间与制作该批号的GM1中间体的2个杂质峰保留值相同。对该批号的GM1干粉和相应批号的GM1中间体中的目标杂质进行半制备级收集,经冷冻干燥除溶剂富集35倍后,用电喷雾-四极杆-飞行时间质谱(ESI-Q-TOF MS)定性分析,对主分子离子峰进行了二级质谱分析。经谱图解析后,推断在GM1干粉和中间体中存在的保留值相同的杂质可能是同种组分。两个杂质峰的结构皆为岩藻糖(Fuc)-GM1,仅是神经酰胺上的长链基团有所不同,峰1的该基团由16个CH<sub>2</sub>组成,而峰2的该基团由18个CH<sub>2</sub>组成。临床数据表明含有上述两种杂质的2批GM1注射液都有副反应,而没有上述杂质的4批GM1注射液都没有临床副反应,而且这两批有临床副反应的GM1注射液都是用同一个批号的含有这两种杂质的中间体制成的,因此推断上述两个杂质可能是引起副反应的主要组分。

**关键词** [高效液相色谱-串联质谱法; 药物中间体; 杂质; 单唾液酸四己糖神经节苷脂](#)

## Separation and identification of the impurities in monosialotetrahexosylgangliosides by high performance liquid chromatography-tandem mass spectrometry

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### Abstract

Comparative analysis of impurities in batches of monosialotetrahexosylganglioside (GM1) powder, injections, and the intermediates for the synthesis of GM1 was performed by using high performance liquid chromatography in order to find out the possible impurities that lead to the clinical side effects. We found that there were two additional peaks in a batch of GM1 powder with retention times that were the same as that presented in the intermediates. The semi-preparative separation and collection of the two impurities in the GM1 powder and intermediates were performed, and then freeze-dried and enriched about 35 times for structure analysis. They were confirmed that the peak 1 and peak 1' were the same compound, and so did the peak 2 and peak 2' by electrospray ionization-quadrupole-time of flight mass spectrometric (ESI-Q-TOF MS) analysis. The structures of the compounds were deduced based on the tandem mass spectra of the main ions, proposed to be fucose-GM1. The two impurities were different on the hydrocarbon chain of the ceramide. The peak 1 has 16 groups of CH<sub>2</sub>, while the peak 2 has 18. The analysis results were consistent with the clinical results for both GM1 powder and injections. It was confirmed that the two impurities were the main cause of the side effects.

**Key words** [Key words: high performance liquid chromatography-tandem mass spectrometry \(HPLC-MS/MS\) intermediate of medicines impurities monosialotetrahexosylganglioside \(GM1\)](#)

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