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Quantitative Determination of Poloxamer 188 in Rat Plasma Using a Specific and High Throughput LC/MS/MS Method  
Aihua Liu, Brandon Wilcock, Laixin Wang, Scott Reuschel and Min Meng

Introduction

Poloxamers are nonionic triblock copolymer surfactants composed of a central hydrophilic phase of poly(oxyethylene oxide) flanked by two hydrophilic chains of polyoxyethylene oxide (Figure 1). Due to their amphiphilic nature and absence of toxicity, they are widely used in pharmaceutical methods for drug delivery systems. However, a small amount of poloxamer 188, when administered to animals, may produce non-specific ionization and elution, which can affect quantification. Therefore, the development of a specific and high throughput LC-MS/MS method is required. In this paper, we describe the development of such a method for quantifying poloxamer 188 in rat plasma.

Methodology

Sources of Materials  
LabCorp Clinical Trials or Tandem Labs

RESULTS

1. LC Program  
A carryover test was executed and no instrument carryover was observed. Column carryover was minimized by forward flushing the column with mobile phase at 0.800 mL/min. A variety of needle wash solvents were observed during method development; in order to minimize the column carryover, different needle wash solvents were chosen. Only phenyl-hexyl columns provided acceptable resolution and sensitivity. Because the duration of UVMS depends on the type of pump used, a Phenyl-Hexyl column was used to ensure acceptable resolution in the matrix. Mobile Phase: A mixture of FA, ammonium acetate, and MeCN was used. Source and Ionization: ESI. Mass Spec: AB Sciex® API 5000. LC Program: Gradient. B: mixture of IPA and MeCN. LC Program: Phenyl-Hexyl. Source Temperature: 500°C. Precipitation Solvent: mixture of MeCN and MeOH. Buffer: Ammonium Acetate. MS Monitoring Parameters:  

2. LC-MS/MS Analysis  
We developed a simple, fast, robust and specific LC-MS/MS assay to quantify poloxamer 188 in rat plasma. We found that poloxamers exhibit poor sensitivity, non-linearity and low selectivity. Here, we developed a method that uses matrix-matched standards and a specific and high throughput LC-MS/MS method to quantify poloxamer 188 in rat plasma.

3. Linearity, precision and accuracy  
The calibration curves were successfully validated over the concentration range of 1.00 – 100 µg/mL in rat plasma. The results indicated that the method is reliable and reproducible. The intra-day accuracy (% bias) and precision (% CV) ranges for three separate samples were 1.00% – 4.40% and 9.00% – 10.7%, respectively. The inter-day accuracy (% bias) and precision (% CV) ranges for three separate samples were 1.92% – 3.90% and 9.00% – 10.7%, respectively. These results demonstrated that the method is suitable and reproducible for the determination of poloxamer 188 in rat plasma.

4. Summary

Conclusion

A selective, fast and robust assay quantifying poloxamer 188 in rat plasma was developed using a protein precipitation extraction and an LC/MS/MS analysis method which used the same grade and from three separate USP/EP solvents.

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