Bioavailability Effect of Methylprednisolone by Polymeric Micelles

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摘要

Abstract

Purpose To investigate the effect of PEO-PPO-PEO polymeric micelles (PM) formulation on the bioavailability of methylprednisolone (MP), a treatment of spinal cord injury (SCI), to the blood and spinal cord (SC) of rabbits.

Methods The characteristic of MP formulated with PM (MP/PM) was evaluated by critical micelles concentration (CMC), dynamic light scattering (DLS), atomic force microscopy (AFM) and in vitro kinetic release measurements. HPLC was used to analyze the MP disposition in plasma and SC of rabbits receiving single dose intravenous administration. After MP/PM delivery, the mRNA and protein levels of anti-apoptotic marker, Bcl-xL, were monitored by Reverse Transcription -Real-Time -Polymerase Chain Reaction (RT-qPCR) and Western blotting analysis, respectively.

Results At a concentration of 0.1% and at 25°C, PEO-PPO-PEO copolymers formed micelles shown by fluorescence probe, DLS and solubility test. The size of the MP/PM was in an average of 60 nm with a single, rounded shape detected under AFM. Being formulated with 6% PM, MP had higher solubility (219.6 ± 3.6 μg/ml) and release rate (11.1 ± 0.4 ng min1/2) at 37°C. After intravenously administrated with single dose of 1 mg/kg of MP/PM to rabbits, higher levels of MP in plasma and SC were detected compared to animals receiving an equal dose of MP, analyzed by HPLC. PM formulation markedly increased (7-fold) the plasma half-lives (t 1/2) of MP (from 76.1 ± 8.0 to 514.3 ± 70.0 min). In addition, the SC t 1/2 of MP/PM also increased from 278 to 528 min. In SC, the mRNA level of Bcl-xL increased 4-fold in animals receiving MP/PM compared to that with MP alone at 7 h post-administration. Similar elevated Bcl-xL protein was also detected upon MP/PM administration compared to MP.

Conclusions PM vehicle was able to deliver MP to improve its pharmacokinetic profile in plasma and SC with higher expression of anti-apoptotic Bcl-xL at both mRNA and protein levels.