



# -Minocycline Block Copolymer Micelles and their Anti Inflammatory Effects on Microglia

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## Abstract:

MH, a semisynthetic tetracycline antibiotic with promising neuroprotective properties, was encapsulated into PIC micelles of CMD-PEG as a potential new formulation of MH for the treatment of neuroinflammatory diseases. PIC micelles were prepared by mixing solutions of a Ca<sup>2+</sup>/MH chelate and CMD-PEG copolymer in a Tris-HCl buffer. Light scattering and <sup>1</sup>H NMR studies confirmed that Ca<sup>2+</sup>/MH/CMD-PEG core-corona micelles form at charge neutrality having a hydrodynamic radius  $\approx$ 100 nm and incorporating  $\approx$ 50 wt.-% MH. MH entrapment in the micelles core sustained its release for up to 24 h under physiological conditions. The micelles protected the drug against degradation in aqueous solutions at room temperature and at 37°C in the presence of FBS. The micelles were stable in aqueous solution for up to one month, after freeze drying and in the presence of FBS and BSA. CMD-PEG copolymers did not induce cytotoxicity in human hepatocytes and murine microglia (N9) in concentrations as high as 15 mg.mL<sup>-1</sup> after incubation for 24 h. MH micelles were able to reduce the inflammation in murine microglia (N9) activated by LPS. These results strongly suggest that MH PIC micelles can be useful in the treatment of neuroinflammatory disorders.

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