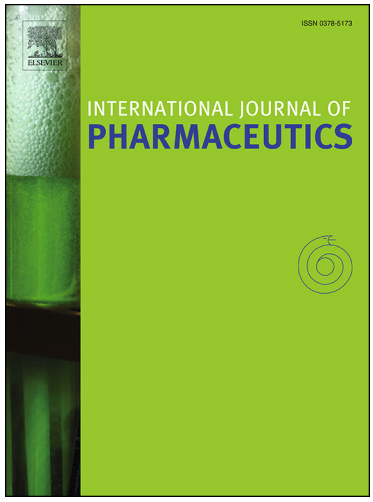

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Nanogel-DFO Conjugates as a Model to Investigate Pharmacokinetics, Biodistribution, and Iron Chelation *In Vivo*

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Abstract

Deferoxamine (DFO) to treat iron overload (IO) has been limited by toxicity issues and short circulation times and it would be desirable to prolong circulation to improve non-transferrin bound iron (NTBI) chelation. In addition, DFO is currently unable to efficiently target the large pool of iron in the liver and spleen. Nanogel-Deferoxamine conjugates (NG-DFO) can prove useful as a model to investigate the pharmacokinetic (PK) properties and biodistribution (BD) behavior of iron-chelating macromolecules and their overall effect on serum ferritin levels. NG-DFO reduced the cytotoxicity of DFO and significantly reduced cellular ferritin levels in IO macrophages *in vitro*. PK/BD studies in normal rats revealed that NG-DFO displayed prolonged circulation and preferential accumulation into the liver and spleen. IO mice treated with NG1-DFO presented significantly lower levels of serum ferritin compared to DFO. Total renal and fecal elimination data point to the need to balance prolonged circulation with controlled degradation to accelerate clearance of iron-chelating macromolecules.