## Accepted Manuscript

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

Yan Wang, Zhi Liu, Tien-Min Lin, Shaurya Chanana, May P. Xiong

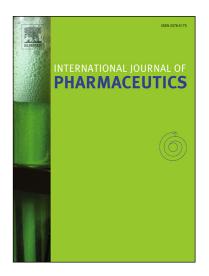
PII: S0378-5173(18)30004-8

DOI: https://doi.org/10.1016/j.ijpharm.2018.01.004

Reference: IJP 17247

To appear in: Indian Journal of Pharmacology

Received Date: 24 September 2017 Revised Date: 14 December 2017 Accepted Date: 1 January 2018



Please cite this article as: Y. Wang, Z. Liu, T-M. Lin, S. Chanana, M.P. Xiong, Nanogel-DFO Conjugates as a Model to Investigate Pharmacokinetics, Biodistribution, and Iron Chelation *In Vivo*, *Indian Journal of Pharmacology* (2018), doi: https://doi.org/10.1016/j.ijpharm.2018.01.004

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

## ACCEPTED MANUSCRIPT

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

Yan Wang<sup>2</sup>, Zhi Liu<sup>1</sup>, Tien-Min Lin<sup>2</sup>, Shaurya Chanana<sup>2</sup>, May P. Xiong<sup>1</sup>,\*

<sup>1</sup>Department of Pharmaceutical & Biomedical Sciences, College of Pharmacy, University of Georgia, Athens, GA 30602, USA

<sup>2</sup>Pharmaceutical Sciences Division, School of Pharmacy, University of Wisconsin–Madison, Madison, WI 53705, USA

\*Correspondence and requests for materials should be addressed to May P. Xiong. E-mail: <a href="mailto:mpxiong@uga.edu">mpxiong@uga.edu</a>

#### 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.

#### Download English Version:

# https://daneshyari.com/en/article/8520318

Download Persian Version:

https://daneshyari.com/article/8520318

<u>Daneshyari.com</u>