Charles O Noble, J Pharm Drug Deliv Res 2016, 5:3(Suppl)
http://dx.doi.org/10.4172/2325-9604.C1.008

Liposome encapsulated Deferoxamine is a more effective iron chelator than Desferal® in an iron overloaded mouse model

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Heart failure is the most common cause of death in children and adults with blood transfusion dependent thalassemia or sickle-cell disorders. This is because long-term transfusions cause an accumulation of iron in the body from the broken down heme in hemoglobin. As humans lack a means of eliminating iron, the iron eventually builds to toxic levels in the vital organs, causing generation of reactive oxygen species followed by cellular apoptosis and necrosis. Chelation therapy is prescribed for patients who have excess iron. Marketed chelators have severe drawbacks. Desferal® (deferoxamine, DFO) requires an infusion time of greater than 40 hours per week. Exjade® and Jadenu® both have black box warnings from the FDA related to renal failure, hepatic failure and GI hemorrhage. Patient compliance is the greatest problem with current chelation therapies. We have devised a novel and stable liposome (LDFO) formulation containing a high concentration of the iron chelator deferoxamine. Toxicology studies show that prototype formulations have no adverse effects well above the therapeutic dose for LDFO indicating that it is better tolerated than Desferal®. Our results show that LDFO efficiently removes iron from the liver and spleens of iron overloaded mice. A single treatment with LDFO results in greater iron excretion than a 14 day continuous infusion of Desferal®. Successful translation of LDFO to patients would result in improved liver iron removal and less frequent dosing than current options.

Biography

Charles O Noble has completed his PhD in Chemistry at Louisiana State University working with conductive polymers and dendrimers. His Post-doctoral work at University of California San Francisco focused on antibody-targeted immunoliposomes and drug delivery to brain tumors. As a Senior Scientist at Merrimack Pharmaceuticals, he was a key contributor to development of a liposomal irinotecan (MM-398) which was approved by the FDA in 2015 for treating pancreatic cancer and is marketed as Onivyde®. In 2011, he has Co-Founded ZoneOne Pharma, Inc., to develop treatments for transfusional iron overload and has the role of President and Scientist. He has co-authored over 40 publications.

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