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Desferrioxamine (Desferal®, DFO), deferiprone (Ferriprox®, L1) and desferasirox (Exjade®, ICL-670) are clinically approved iron chelators used to treat transfusion associated iron overload; a common condition in patients with severe hemoglobin disorders like β-thalassemia, sickle-cell disease and the myelodysplastic syndromes. The poor pharmacokinetics and inefficacy of iron chelators necessitate administration of almost maximum tolerated doses to achieve adequate iron removal.

This causes toxicity ranging from neurological dysfunction in DFO users, agranulocytosis and neutropenia in L1 users, and severe kidney toxicity in ICL-670 treated patients. This also hinders the use of iron chelators during gestation. Thus, developing iron chelators with improved long-term efficacy and reduced toxicity is essential.

All currently approved iron chelators are of low molecular weight (MW) (<600 Da) and the objectives reported for the "ideal" chelator of low MW is yet to be realized in practice. However, the limited attempts towards developing higher MW, long circulating iron chelators has shown tremendous promise. This thesis assesses the role of a new polymer, hyperbranched polyglycerol (HPG) in improving the properties of iron chelators.

High MW iron chelators were developed by conjugating DFO to HPG of various MWs, forming a library of HPG-DFO conjugates. Iron binding affinity of HPGDFO was investigated using isothermal titration calorimetry, UV-visible spectroscopy and studying iron removal from ferritin. Biocompatibility and toxicity were investigated using coagulation assays in human blood and cell culture.

Since iron chelator toxicity during development remains an under-explored area, the second goal of this thesis was to expand knowledge of chelator toxicity during development. The toxicity of FDA-approved and HPG-DFO in developing embryos was investigated using zebrafish.

Studies indicate that HPG-DFOs are biocompatible, efficient chelators, capable of removing ferritin iron and preventing harmful redox reactions. Moreover, combining a low MW iron chelator with HPG-DFO enhances chelation. *In vivo* chemical screening indicated that while low MW chelators L1 and ICL-670 may interact with zebrafish embryos and cause toxicity, DFO and HPG-DFO did not have this effect. Results indicate that HPG-DFO is a new class of efficient, biocompatible iron chelator, potentially useful for development into clinical agents for the prevention of transfusion associated iron overload.