Non-toxic iron chelators designed to remove excess iron from inside cells

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Pharmaceuticals

Problem

Patients with beta-thalassemia undergo frequent red blood cell transfusions to combat life-threatening anaemia, resulting in iron-overload disease where excess iron accumulates in the body and vital organs, risking serious damage. Lacking a natural iron excretion mechanism, these patients must use iron chelators daily to bind and eliminate the excess iron.

Three iron chelators (DFO, DFX, DFP) with variable properties are available for treating iron overload disease. DFO has a good safety profile and is the most effective in removing iron from plasma. However, it cannot remove iron from inside cells and is administered by infusion rather than by mouth. DFX and DFP are orally administered and can remove iron from plasma and from inside cells but have toxicity risks (some quite serious) which pose concerns for lifelong treatment.

Patients could benefit from an iron chelator that is non-toxic, has a tolerable administration regimen, and that is effective at removing iron from plasma and from inside cells.

Solution

The University of Sydney has invented the DFL class of iron chelators to address this clinical need. The DFL iron chelators have an on-paper toxicity profile similar with non-toxic DFO. The DFL iron chelators are designed to remove iron from plasma and from inside cells.

This property would confer functional superiority upon DFL compared to DFO, since iron stored inside cells is the major cause of morbidity and death in patients with iron overload disease.

The DFL chelators are predicted to have a longer residence time than DFO, which could translate to a dose reduction and a shorter administration time to improve patient adherence and overall treatment outcomes.

Intellectual Property Status

Provisional Patent (University of Sydney) filed November 2023.

Potential Commercial Applications

The DFL iron chelators could be used to treat

— secondary iron overload in patients with transfusion-dependent blood disorders. These include beta-thalassemia and sickle cell disease.

— myelodysplastic syndrome (rare blood cancers involving the production of insufficient healthy blood cells) who can require blood transfusions and iron chelation therapy.

— acute iron poisoning. DFO is the current first-line treatment used in this setting. Each year in the US, there are about 5,000 cases involving acute iron poisoning in children who have accidentally swallowed iron tablets.

Methods of production of the DFL chelators have identified potential opportunities to produce DFO by chemical synthesis rather than as a fermentation product.

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