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The recovery of Oxyhaemoglobin in haemolysate by Desferal (DFO) and Defriprone (L1) that are currently in clinic use for the treatment of transfusional iron overlaod in beta thalassemia major patients

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The development of potent metal chelators has a great benefit in medicine, agriculture and industry. Surprisingly, the clinically use of defriprone (L1) in synergism with desferal (DFO) as potent metal chelators for the treatment of iron (III) overload in thalassemic patients, has additional clinical applications such as inhibiting prostate cancer proliferation at clinically relevant doses and plasma concentrations. Furthermore, the bidentate ligand L1 and hexadentate ligand DFO exhibit a great effect by recovering the oxyhaemoglobin from the iron-mediated oxidative damage on oxy-haemoglobin in haemolysed red blood cells after five minutes of iron addition (data not published yet). In this work, physical and chemical properties (pKas and β) values of L1 and DFO were used to theoretically show the potential of DFO over L1 in complexing iron (III). These simulations might offer an insight into which compound recovers faster the oxidative damage from oxyhaemoglobin that occurs in blood haemolysate associated with an accumulation of iron (III). This study shows that 0.5 mM DFO recover 95% of the oxidative damage of oxyhaemoglobin faster than that of 0.5 mM L1. This was measured by monitoring the absorbance in the visible region between 500 nm and 800 nm of the oxyheamoglobin with varying concentrations of iron (III) from 50 μM to 250 μM in 50 increment steps at physiological pH using 50 mM phosphate buffer in the presence and absence of L1 and DFO. The potential medical application of these compounds would be useful to prevent oxidative damage that occurs as a result of red blood cell haemolysis with the commensurate release of oxy-haemoglobin, that contributes to acute and chronic vascular disease, inflammation, thrombosis, and renal impairment.

Biography

Hicham H Khodr obtained his PhD in NMR studies of ligand-Ferritin interaction. He is an expert in NMR spectroscopy and programming. He had developed an autotitration system at King's College London Pharmacy, UK. This system enables us to study the physicchemical properties of many compounds that of agriculture and clinical uses. Furthermore, he worked with Prof. Hider group at KCL, Pharmacy in the area of synthesis and characterization of new candidate compounds as pro drug for the treatment of b-thalassemia major. His major target is to develop new candidate compounds (bidentate and tetradentate) for preventing the oxidative damage in red blood cell haemolysis as well as for the treatment of β-thalassemia major.

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