

## The Effects of Deferiprone and Deferasirox on the Structure and Function of $\beta$ -Thalassemia Hemoglobin

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### Abstract

Transfusional iron overload is a major cause of morbidity and mortality in thalassemia, sickle-cell disease and other chronic anemias. To overcome these problems, orally bioavailable iron chelators, deferiprone and deferasirox, were used for the treatment of patients suffering from thalassemia. The interactions between deferiprone and deferasirox with the carrier protein,  $\beta$ -thalassemia hemoglobin (Hb), were investigated using fluorescence, circular dichroism (CD) and UV-visible measurements at physiological condition.

Strong fluorescence quenching on interactions of the above drugs with  $\beta$ -thalassemia Hb were observed. Fluorescence quenching data of thalassemia Hb in the presence of deferasirox have shown greater affinity of binding. The number of binding sites to Hb for deferasirox was found to be more relative to those of the deferiprone. The effects of these drugs on the oxygen affinity of the thalassemia Hb were studied by spectroscopic methods using sodium dithionite. Results indicated that deferiprone reduces oxygen affinity (increases oxygen releasing ability) of Hb, while in the presence of deferasirox, oxygen affinity of Hb has significantly increased by dose-dependent manner. As such, deferasirox exhibited opposite effect relative to deferiprone on the function of thalassemia Hb. In clinical dose of deferiprone, CD results showed that, the  $\alpha$ -helical content of thalassemia Hb significantly increased. By use of the clinical dose of deferasirox, however, a decrease in  $\alpha$ -helical content of protein was observed, which resulted in decreasing stability of thalassemia Hb. Our study showed that reduction in stability of thalassemia Hb in the presence of deferasirox induced higher conformational changes in protein.

**Key words:** Deferiprone; Deferasirox;  $\beta$ -thalassemia Hemoglobin; Oxygen affinity; Circular dichroism.

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**Abbreviations:** Hb: Hemoglobin; CD: Circular dichroism; Trp: Tryptophan; SDT: Sodium dithionite.