

## Effect of Purified Poloxamer 188 or Various Dextrans on Erythrocyte Sedimentation Rate in Patients with Sickle Cell Disease

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**Background:** Purified poloxamer188 (MST-188) (Mast Therapeutics) is a non-ionic, linear block copolymer composed of a central chain of hydrophobic polyoxypropylene and two flanking chains of hydrophilic polyoxyethylene (MW 8.5 kDa). This agent has hemorheologic properties which result in improved microvascular blood flow. It is currently under study in an international phase 3 clinical trial in sickle cell patients with vaso-occlusive crisis. Dextrans are branched polysaccharides of 10-70 kDa that have been used as antithrombotic agents and plasma expanders. The erythrocyte sedimentation rate (ESR) is reflective of red blood cell (RBC) aggregation and has been shown to be elevated during vaso-occlusive crisis. This study compares the effect of MST-188 and various dextrans on ESR's in blood obtained from patients with sickle cell disease presenting at Loyola University Medical Center clinics.

**Methods:** EDTA anticoagulated whole blood collected from normal individuals (n=8) and sickle cell patients (confirmed by electrophoresis) (n=11) was supplemented with MST-188 or dextran 10K, 18K, 40K and 70K at various concentrations (or saline control). ESR was measured using a standard laboratory technique.

**Results:** ESR's for sickle cell patients ( $26.4 \pm 7.1$  mm/hr) were significantly elevated in comparison to those for healthy subjects ( $14.6 \pm 2.1$  mm/hr). Addition of MST-188 to sickled blood decreased the ESR's to  $14.1 \pm 4.6$  mm/hr ( $\Delta 47\%$ ). In contrast, comparable concentrations of dextrans showed little or no effect on the sickle blood ESR

**Conclusions:** Previous investigators have shown that ESR is elevated in sickle cell patients during vaso-occlusive crisis. MST-188 (but not any dextrans) decreased (up to 50%) elevated ESR's in sickle cell blood. This may be due to inhibition of acute phase reactant induced RBC aggregates resulting from the effect of MST-188 on RBC membranes or cell-protein interactions. Since none of the dextrans produced a similar decrease, the observed lowering of ESR by MST-188 is unlikely a non-specific effect related to polymer molecular weight. Lowering of an elevated ESR with MST-188 reflects reduced sickle RBC aggregation and is suggestive of improved microvascular blood flow.