

## USE OF A NOVEL IRON CHELATOR (HBED) IN BLACK RHINOCEROS

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### **Abstract**

Black rhinoceroses (*Diceros bicornis*) are critically endangered and are compromised by iron overload under human care (Paglia and Tsu, 2012; Molenaar et al., 2008). With the goal of safely reducing iron absorption in the gastrointestinal tract of affected and susceptible individuals, we investigated oral administration of the iron chelator, N,N-bis(2-hydroxybenzyl)ethylenediamine-N,N-diacetic acid (HBED) to 2.1 black rhinoceros. We expected HBED administration with diet to increase iron excretion, without compromising the health of the black rhino as assessed by blood parameters. Previously, HBED was tested thoroughly for toxicity and iron elimination efficacy in rats, non-human primates, dogs and through phase 1 clinical studies in humans (Bergeron, 1999; Grady and Hersko, 1990; Grady, 1994). Furthermore, our study was completed after our successful safety and efficacy study in the horse (Sullivan et al., 2014), the most appropriate digestive model for black rhinoceroses (Clauss et al., 2007). In the black rhinoceros study, we used a crossover design to compare iron excretion with and without HBED (40 mg/kg BW/day). Rhinos consumed 100% of HBED or control dosed with the diet. Rhinos excreted significantly more iron in the urine when administered HBED ( $349 \pm 57$  ng/ml) versus control ( $78 \pm 13$  ng/ml;  $P < 0.05$ ). Fecal iron excretion was not significantly different between treatments. The males did not show changes in serum parameters, but were not considered highly overloaded during the study. While HBED successfully sequestered and excreted iron via the urine and appeared to immediately decrease serum iron saturation in the iron-overloaded female, medical complications in the female animal's case raise concern about the safety of HBED administration in iron-overloaded individuals (Sullivan et al., 2015). Although demonstrated efficacy of this chelation treatment could potentially prevent or manage iron overload in black rhinos under human care, extra caution should be taken before further testing is initiated in compromised and/or iron-overloaded individuals. Iron overload disorder threatens the health and survival of black rhinos managed under human care, and research must be continued to find the safest effective methodology.

### **Acknowledgements**

The authors would like to thank Morris Animal Foundation for the funding for this project. Thanks to all of the Nutrition Team that aided in full collections, including Scott Williams and Katherine Kerr; as well as the assistance of the entire Disney Ituri Team, especially Roxane Losey, Mauricio Saldarriaga, Jeremy Neufeld, Brandy Coffin, Michelle Corcoran, Chad Harmon and Kristin Wolfe.

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