

2,4-DIAMINOQUINAZOLINES AS ANTI-LEISHMANIALS

Kurt S Van Horn¹, Xiaohua Zhu², Trupti Pandharkar², Brian Vesely³, Sihyung Yang⁴, Dennis Kyle³, Michael Zhuo Wang⁴, Karl Werbovetz², Roman Manetsch¹

¹ Chemistry Department, University of South Florida, 4202 E. Fowler Ave. CHE 205, Tampa, FL, 33620

² Division of Medicinal Chemistry and Pharmacognosy, Ohio State University, Columbus, Ohio 43210

³ Department of Global Health, University of South Florida, Tampa, FL, 33620

⁴ Department of Pharmaceutical Chemistry, University of Kansas, Lawrence, Kansas 66047

Leishmaniasis is a protozoan parasitic disease that puts 350 million people at risk in 88 countries. It is caused by more than 20 species of the genus *Leishmania*. We have synthesized and analyzed the anti-leishmanial properties of a set of 2,4-diaminoquinazoline analogues. These compounds have been found to display single digit micromolar or high nanomolar activity against intracellular *Leishmania donovani* in vitro and also possess selectivity indexes >20 (toxicity against J774 macrophages/activity against intracellular *L. donovani*), making these compounds interesting leads. One 2,4-diaminoquinazoline in this series also displays efficacy in our murine model of visceral leishmaniasis, reducing liver parasitemia by 36% when given by the intraperitoneal route at 15 mg/kg/day for five consecutive days.