PRELIMINARY STUDY FOR
GIARDIASIS DRUG DEVELOPMENT

Brandi Tredeau, Bethany Bleich, Cindy Konopasek and Chun Wu
Division of Natural Sciences
Mount Marty College
Yankton, SD 57078

ABSTRACT

Giardiasis is the most common form of non-bacterial diarrhea in North America. It is caused by the parasite *Giardia lamblia*. *Giardia lamblia* is classified as a category B organism in response to bioterrorism threats by the Centers for Disease Control and there are over 2.5 million cases of giardiasis occur annually in the United States. Currently there is no FDA approved medicine available. The long-term goal of this project is to develop new drug candidates for alternative treatments of Giardiasis.

Class II *Giardia* fructose-1,6-diphosphate aldolase catalyzes the reversible condensation of dihydroxyacetone phosphate with glyceraldehyde 3-phosphate to produce D-fructose 1,6-bisphosphate in glycolisis, a central metabolic pathway. Class II Giardia fructose-1, 6-diphosphate has been shown to be essential to *Giardia lamblia* growth by RNAi gene knock-out experiment. In addition, this enzyme does not exist in human cells. Therefore, it is an ideal anti-parasitic drug target.

This poster reported on the rational design of *Giardia* aldolase inhibitors. A novel active site filling model was applied. It included molecular modeling via a Linux workstation (e.g. Insight II, Autodock 3.0 and Ludi). The synthesis of major intermediates of those candidates was reported.

The future work will include in-*vitro* inhibitor evaluation (e.g. layout of bioassays, Michaelis-Menten kinetics, Lineweaver-Burk plots and enzyme inhibition, etc.). Once a nanomolar level inhibitor with high specificity is identified, development of the X-ray crystal structure of enzyme inhibitor complex will be performed followed by in-*vivo* evaluation.