

ABSTRACT

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Pharmacology and Toxicology

Student: Anna Odvárková

Supervisor: RNDr. Jakub Hofman, Ph.D.

Consultants: Carina Lemke

Prof. Dr. Michael Gütschow

Title of diploma thesis: Kinetic Evaluation of Potential Inhibitors for Selected Cysteine Proteases

Cysteine cathepsins are proteases which are naturally present in the human body, taking part in various physiological processes such as cell signaling, proliferation or bone remodeling. However, their dysregulation leads to serious disorders. An aberrant activity of cysteine cathepsins is present in diseases like cancer, osteoporosis, neurodegenerative disorders or autoimmune diseases. Therefore, these enzymes can serve as valuable diagnostic or therapeutic targets. Rhodesain is a parasitic protease produced by *Trypanosoma brucei rhodesiense* and essential for its survival. This enzyme shares a high homology with human cysteine cathepsin L. Inhibition of rhodesain can be a potential treatment of African trypanosomiasis, also known as sleeping sickness.

Inhibitory potency of several compounds against the target enzymes was assayed spectrophotometrically or fluorometrically and the results were evaluated by using linear or non-linear regression. Determination of a Michaelis-Menten constant for rhodesain under specific assay conditions was also performed. Some potent inhibitors of tested proteases have been identified and additionally, a potential activity-based probe was investigated for its applicability in sodium dodecyl sulfate polyacrylamide gel electrophoresis.