Candida parapsilosis is an opportunistic fungal pathogen of humans causing a variety of infections. Immunocompromised individuals represent the most threatened group of patients. The increasing frequency of infections and occurrence of drug resistant strains are the main reasons for research focused on novel antimycotic compounds. Inhibition of secreted aspartic proteases (Sap) of pathogenic Candida spp. appears to be a potential target of therapeutic intervention. The genome of C. parapsilosis contains at least three genes coding for secreted aspartic proteases, denominated SAPP1-3. Protease Sapp1p has been well biochemically and structurally characterized, whereas Sapp2p and Sapp3p have been given less attention. The first part of the thesis is focused on structural analysis of Sapp1p complexes with selected peptidomimetic inhibitors binding to the active site of the enzyme. In addition, complex of the isoenzyme Sapp2p with the well-known secreted aspartate inhibitor Pepstatin A has been analyzed.

The second part is related to the fact that C. parapsilosis belongs to the Candida spp. with the unique ability to translate standard leucine CUG codon mostly as serine. Even though it is a non-conservative substitution of hydrophobic amino acids for a hydrophilic one, this unique ability is maintained for more than 170 million years. Some studies have focused on selective advantages and consequences of alternative CUG codon usage to the overall phenotype of the yeast. However the effect on the structure and function of specific proteins is less known. The second part of the thesis aims to clarify the impact of alternative CUG codon usage on the structure and function of protease Sapp1p whose nucleotide sequence includes one CUG triplet. The resulting serine is located in a loop near the active site in the structure of Sapp1p.