FROM INHIBITORS OF THE SECRETED ASPARTIC PROTEASES (SAPS) OF *CANDIDA ALBICANS* TO NEW FALCIPAIN INHIBITORS

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Proteases play pivotal roles in the pathogenesis of various diseases. Examples are the secreted aspartic proteases of the fungus *C. albicans* (SAPs) which are key virulence factors, and promising targets for new antimycotic drugs. In the search for new irreversible inhibitors we developed *cis*-configured aziridines which were shown to exhibit a dual pseudo-irreversible inhibition mode. Molecular modeling studies suggested hybrid inhibitors targeting an aspartic acid residue unique in the SAPs, thus enhancing selectivity towards SAPs within the family of pepsin-like aspartic proteases. However, these new compounds did not inhibit aspartic proteases, but surprisingly the Boc-protected intermediates of the syntheses exhibited inhibitory potency against cysteine proteases of the protozoa *Plasmodium falciparum*, falcipains 2 and 3. These enzymes are the major hemoglobinases of the parasite and are considered new targets for antimalarial drugs. Syntheses, docking studies and biological activities of the inhibitors will be presented.
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