EVALUATION OF ANTI-*TOXOPLASMA GONDII* ACTIVITY OF ASPARTIC PROTEASE INHIBITORS

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Toxoplasmosis, caused by the protozoan *Toxoplasma gondii*, affects approximately one-third of the global population and can lead to severe complications, such as congenital, ocular, and neurological disorders. The treatment of toxoplasmosis is hindered by significant limitations, particularly concerning efficacy and safety, underscoring the urgent need for new drug development. Aspartic protease inhibitors are compounds with previously documented activity against protozoa and viruses, including *Plasmodium*, *Leishmania*, and HIV. In *T. gondii*, seven genes encode aspartic proteases, with TgASP1, TgASP2, and TgASP5 expressed during the parasite's infectious stage. This study aimed to investigate the anti-*T. gondii* activity of underexplored aspartic protease inhibitors. Seventeen inhibitors were evaluated in *in vitro* assays against intracellular tachyzoites of *T. gondii* (RH strain) and human foreskin fibroblasts (HFF). Effective concentration (EC_{50}), cytotoxic concentration (CC_{50}), and selectivity index (SI) values were determined to identify compounds with selective activity. Additionally, absorption, distribution, metabolism and excretion (ADME) predictions were performed to select compounds with favorable pharmacokinetic and pharmacodynamic profiles. The investigated inhibitors exhibited EC_{50} values ranging from 0.9 to 40 μM and CC_{50} values from 4.9 to 257 μM, resulting in SI up to 34. Among the evaluated inhibitors, twelve compounds demonstrated desirable ADME characteristics, including one compound with documented activity and efficacy against *Plasmodium*. To further explore the therapeutic potential of these inhibitors for toxoplasmosis, future studies should focus on elucidating their mechanism of action and validating their *in vivo* efficacy.

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