INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Programme of Study	:	Ph.D.
Thesis Title	:	Studies on calcineurin and calcium ATPase PMR-1 roles in azole drug susceptibility in *Neurospora crassa*, and their interactions with azoles and phytochemical compounds
Name of Thesis Supervisor(s)	:	Prof. Ranjan Tamuli
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SHORT ABSTRACT

This thesis describes the effect of azoles in *Neurospora crassa*, and the molecular basis of interactions of the calcineurin and PMR-1 proteins with the fluconazole, itraconazole, and ketoconazole drugs. Azole treatments reduced ergosterol levels and increased reactive oxygen species (ROS) in the *N. crassa* calcineurin and *pmr-1* mutant strains. In addition, field emission scanning electron microscopy (FESEM) analysis revealed altered hyphal morphology in the calcineurin RIP and Δ*pmr-1* mutants treated with the azole drug fluconazole. Furthermore, expression of the *pmr-1* was upregulated under itraconazole treatment. Molecular docking and molecular dynamics (MD) simulations revealed the stable interactions of the azole drugs within the active site of the protein calcineurin and PMR-1 with efficient binding energies. Preliminary computational insights also show the critical amino acid residues for drug-target interactions. In addition, this study also delves into phytochemical compounds as potential inhibitors against Ca^{2+} signaling proteins pivotal in fungal pathogenicity, using computer-aided drug design (CADD). A total of 11 phytochemicals were assessed for their inhibitory potential, adhering to Lipinski's rule of drug-likeness, and *in silico* studies identified isorhamnetin as a promising phytochemical inhibitor for PMR-1 and CNA-1 proteins and dillenetin as a potential inhibitor of CNB-1 protein

with the formation of the most stable complex. In conclusion, this thesis enhances our understanding of the molecular basis of azole susceptibility in *N. crassa.* The study also provides a promising future for the development of target-specific new antifungals targeting calcineurin and PMR-1.