INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Programme of Study	:	Ph.D.

Thesis Title: Xanthine Based Inhibitors for Therapeutics Targeting Phosphodiesterase 9A

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Xanthine is a versatile nitrogenous alkaloid. The pharmaceutical active nature of xanthine derivatives is widely known for treating various diseases. Therefore, xanthine can act as structurally rigid scaffold which provides enormous possibility for molecular diversity in drug development process. Xanthine based compounds are reported for their non-specific phosphodiesterase inhibition, however, xanthine based inhibitors have not been reported for PDE9A inhibition. With introduction of "xanthine" as a scaffold, the present study was an attempt to bring molecular diversification in PDE9A research. The current study was emphasized on two approaches – one was virtual screening to find out the possibilities of existing xanthine based derivatives to regulate the catalytic action of PDE9A and the second approach was to use the xanthine as scaffold for designing new xanthine derivatives and again the same xanthine was used as 'starting material' for synthesizing selected xanthine derivatives. Two schemes were developed based on getting clear understanding over the molecular structure of xanthine. The biological studies were carried out to understand the biological affinity of the selected virtual screened compounds and chemically synthesized new compounds by using spectrophotometric inhibition studies for structural activity relationship (SAR) analysis and thermal shift assay for stability studies of protein-ligand complex. The biological studies showed chemically synthesized xanthine derivatives as better inhibitors than virtual screened compounds.