



INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Thesis Title: Development of Immunosuppressive Indoleamine 2,3-dioxygenase 1 Inhibitors for Chemolmmunotherapeutic Advancement
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SHORT ABSTRACT

This thesis “Development of Immunosuppressive Indoleamine 2,3-dioxygenase 1 Inhibitors for Chemo-Immunotherapeutic Advancement” deals with small molecules for the immunotherapeutic treatment in life threatening disease. This thesis has been arranged into five chapters based on the experimental results which were obtained during the research period.

Chapter 1 elaborates the functions of indoleamine 2,3-dioxygenase 1 (IDO1) enzyme in cancer. This chapter also discusses the importance of developing small moleculebased inhibitors for the domain, IDO1 and gives a small overview of reported inhibitors up to date.

Chapter 2 describes 1*H*-indazole derivatives as a suitable inhibitor of IDO1 enzyme. This chapter has explored that C3-substitution in indole ring generates the substrate, L-tryptophan alike motif which binds with active pocket to behave as antagonist of the enzyme.

Chapter 3 elucidates histidine mimic triazole derivatives which binds with prosthetic heme group in the IDO1 active pocket to show potent inhibitory activity. In addition, rejuvenation of IDO1 mediated immune-suppression with potent triazoles has been discussed in this chapter. In vivo antitumor efficacy of the triazole derivatives also has been conversed.

Chapter 4 articulates quinine-based apo-IDO1 targeting inhibitors which displayed robust and selective inhibition in lower nanomolar concentration range. In this chapter, perturbation of IDO1 activity by aqueous heme-inhibitor complex has been exemplified for the first time.

Chapter 5 conveys a comprehensible outcome of a delivery vehicle which has selectively delivered chemo and immunotherapeutic, IDO1 inhibitor into the cancer cells. The induction of immunogenic cell death (ICD) by both chemo and immunotherapeutic drugs in *in vivo* model has been reflected in this chapter.