ABSTRACT

Gastric Cancer is the third most leading causes of cancer deaths in the world (source: World Health Organization). It is a source of major concern, especially for the developing countries. It is caused due to formation of malignant cells in the lining of stomach. One of the major causes of gastric cancer is *Helicobacter pylori* infection. Although many drugs have been proposed for eradication of *H.pylori* like clarithromycin, tetracycline etc. but the effectiveness is challenged either due to side effects or antibiotic resistance in bacteria. This calls for the need of novel therapeutic discoveries.

One of the good targets for antimicrobial therapeutics is IMPDH enzyme. Structurally this enzyme is a tetramer and has a square planar geometry. It contains two domains: CBS domain and the catalytic domain, and the protein is 481 amino acid long. IMPDH enzyme is involved in one of the major biochemical reactions for life- synthesis of guanine nucleotide (specifically the step of conversion of IMP to XMP). The rationale behind using this enzyme is that: it is involved in one of the major biochemical reactions for life- synthesis of guanine nucleotide, and also there is structural difference in both eukaryotic and prokaryotic IMPDH, therefore, the inhibitors of *H. pylori* IMPDH would not affect the human host.

In this project we have analyzed several molecules using in vivo inhibition assays. The protein was expressed, and isolated using affinity chromatography followed by FPLC to ensure the purity of the protein. The inhibition assays were done using plate reader, and the NADH fluorescence was quantified to find the progression of reaction. The IC_{50} values were used for the comparison of molecules.

Following the in- vitro analysis, in vivo toxicity studies were performed on *Danio rerio.* The zebrafish model was validated using amino acid sequence comparison of zebrafish IMPDH to human IMPDH and *H. pylori* IMPDH using BLAST. The toxicity was tested on four concentrations of the compounds that showed promising in-vitro results of inhibiting *H. pylori* IMPDH, using this model organism.